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American Journal of Diseases of Children

VOLUME 30 DECEMBER, 1925 NUMBER 6

THE CONDITIONED REFLEXES AND CHILDREN'S NEUROSES *

N. I. KRASNOGORSKI, M.D.
LENINGRAD, RUSSIA

Though our knowledge of the activity of the brain dates back to the middle of the last century and important facts about that activity had already been discovered, all those single facts did not comprise all phenomena of the highest nervous activity of the animal, and did not let us understand the physiologic mechanism of its behavior as a whole.

The systematic study of the function of the cerebral hemispheres, as an organ of the highest nervous activity of animals by the purely physiologic method of conditioned reflexes, was begun by Prof. I. P. Pavlov [1] in 1901. It is known that Professor Pavlov proposed to make use of the reflex of the salivary glands as a reaction of the animal to external stimuli, and proved that this reflex, by means of the associative mechanism of the cortex, will respond to numerous external stimuli. The external stimuli could produce salivation, as a conditioned reflex, if they coincided several times with the activity of the salivary glands. For these investigations special laboratories were built, in which all stimuli could be more or less precisely determined. Purely physiologic problems were given to the investigators, and the facts obtained were arranged in physiologic systems and analyzed in a strictly physiologic way.

This new method furnished important results, and we now have a new section of the physiology of the cerebral hemispheres which is absolutely independent of psychology. It is based on a firm, biologic foundation; it permits us to understand the mechanism of the animal's behavior as a whole, and it opens a large field for further researches.

FIRST INVESTIGATIONS

The first investigations of conditioned reflexes in children were made by me in 1907,[2] inspired by Professor Pavlov's researches, his reports and his lectures on conditioned reflexes with animals. As an external

* Received for publication, Aug. 8, 1925.

* From the Clinic of Children's Diseases of the Medical Institute.

1. Pavlov, I. P.: Twenty Years' Experience of the Objective Study of the Highest Nervous Activity (Behavior) of Animals, 1923.

2. Krasnogorski, N. I.: An Experiment of Formation of Artificial Conditioned Reflexes with Infants, Russkiy Vratch, **36,** 1907.

reaction of the child to external stimulation, I proposed to use the motor reflex of the opening of the mouth. I formed the conditioned reflexes by means of a food reflex. At the present time, many of my colleagues take part in this work, and our method is being improved. The laboratory in which the experiments are being made allows us to isolate the child from the experimenter; we carefully avoid indirect casual irritations, and not a word is uttered during the experiment. All stimulations causing conditioned reflexes and also feeding are realized automatically. The motor reaction, the moments of the beginning of stimulation and those of feeding are registered on the ribbon of a kymograph. Sometimes we register the pulse, breathing and blood pressure. In the motor reaction we measure the latent period, the time of increase of the curve to its highest point, its height, durability and superficial extent. From this we can judge the size, intensity and character of the conditioned reflexes with sufficient accuracy.

In the course of our work, we [3] have learned that in America psychologists are carrying on experimental investigations which are akin to our studies. From the time of Edward L. Thorndike's classical work on "Associative Processes in Animals," this new teaching—behaviorism—began to develop on a large scale. The American penetrating and practical mind saw that it is more profitable to know precisely the visible and external reactions of the organism than to be imagining its internal psychic processes. The behaviorists tried to explain the external reactions in purely objective terms, and subjective interpretations were carefully avoided. "Psychology, as the behaviorist views it, is a purely objective, experimental branch of natural science, which needs introspection as little as do the sciences of chemistry and physics" Watson.[4]

With regard to human beings, R. M. Yerkes holds the following view: "Human behavior is only a part, albeit a most important part, of the materials of the general science of organic behavior. It presents essentially the same kinds of problems as does the behavior of any other animal; and it must be studied by methods similar to, if not actually identical with, those emphasized by the student of infrahuman behavior."

CONDITIONED REFLEXES

The conditioned reflexes in children were studied in America by Florence Mateer [5] inspired by William H. Burnham's lectures. She

3. Krasnogorski, N. O.: Ueber die Bedingungsreflexe im Kindesalter, Jahrb. f. Kinderh. **69**, No. 1, 1908.

4. Cited by Pavlov, footnote 1.

5. Mateer, Florence: Child Behavior: A critical and experimental study of young children by the method of conditioned reflexes, Boston, 1918.

has attained important results and has verified that our method is valuable for studying the normal and defective child.

She writes as follows:

"In the case of children, whom other tests leave undiagnosed or unprognosed these methods indicate a procedure which makes a more fundamental test of the mental processes, and consequently they discriminate potential defectives and psychasthenics in a way that is more highly prognostic than are the results of any other test now employed."

The functions of the cerebral hemispheres, as shown by Professor Pavlov, have all the features of reflex activity. However, the reflexes of the cortex are infinitely more complicated than those of the other parts of the nervous system. If the reflexes of the lower sections of the central nervous system are simple, permanent, innate, belonging to the species, appearing in all conditions, that is, absolute, nonconditioned reflexes, the cortical reflexes are complex, temporary, acquired in life, individual and variable according to external conditions; these are conditioned reflexes. These reflexes are conditioned because they can be formed only when the external stimulation has coincided several times with some activity of the animal. Constantly being formed anew, dependent on the perpetual vacillations of the surrounding medium and being a highly sensitive evolutionary mechanism, the conditioned reflexes constitute the most complicated and expedient relations between the organism and the external world.

Formed in the process of adaptability to the constantly new stimulations experienced in life, the conditioned reflexes are themselves always changing—becoming stronger or weaker, being extinguished and reconstructed or disappearing. These perpetual changes of conditioned reflexes are dependent on the development of cortical inhibition.

The inhibitory functions of the cortex manifest also all characteristics of reflex activity. The formation of the inhibitory reflexes and on no less a scale those of conditioned reflexes is realized in the cerebral hemispheres. The inhibitory reflexes are formed and can exist in the same manner as other conditioned reflexes, that is, only for a certain time and under strict conditions. Now we know that every external agent can acquire the function of inhibiting some activity if its action coincides several times with the cessation of this activity. The physiologic effects of inhibitory reflexes consist in inhibiting those activities, to which they are also in constant vacillation, either being strengthened or weakened by the irritative process.

Every conditioned reflex or cortical inhibitory reflex influences the whole activity of the cerebral hemispheres. Each of these reactions excites the irritative or inhibitory process, which spreads over the cortex, increasing or decreasing its general tonus. But the excitability of the cortex is influenced also by the constant starting of reciprocal

induction, that is, by irritation-inhibition (negative induction) and by inhibition-irritation (positive induction).

Thus all the activity of the cerebrum is composed of an innumerable quantity of conditioned reflexes and cortical inhibitory reflexes, and of their subsequent effects, caused by radiation and reciprocal induction. These two kinds of conditioned reactions with opposite functions balance each other, and on their precise equilibrium is based the normal function of the cerebral hemispheres. Any change of this balance immediately influences the intensity and the character of the conditioned reflexes; pronounced and permanent disturbances produce pathologic changes of the highest nervous activity.

In a series of experiments at the laboratory of Professor Pavlov,[6] many cases of disturbances of the balance between irritation and inhibition in dogs were investigated by Drs. D. S. Fursikov, M. K. Petrova, I. P. Rosenkov, V. A. Krilov, A. D. Speransky and L. N. Fedorov. As Professor Pavlov has proved, a disturbance of the balance developed when a task which was too difficult was given to the animal; dogs show here two different reactions: some of them develop a general inhibition, while others show extreme excitement.

In our study of conditioned reflexes in children, our attention was also drawn to the changes in the conditioned reflex activity and in the whole behavior of the child when we made the relationship between irritation and inhibition difficult. As we consider that the investigation of these changes may be important for the clinic and for pedagogy, we made several special experiments on this subject.

RESULTS

When working with Dr. J. K. Panferov,[7] I saw some symptoms in a child during the formation of difficult differentiations of acoustic rhythmical stimuli.

We formed in the child, I. N., aged 6, a conditioned reflex from the metronome. When the reflex was stabilized, we began to differentiate ninety-two from 144 beats. The sound of 144 beats was constantly being accompanied by feeding and occasioned the conditioned motor reflex; the stimulator 92 was inactive, because the child never received food with it. This differentiation was soon formed by the child, that is, after not having been given food six times with ninety-two beats of the metronome. After that, we made differentiations which

6. Pavlov, I. P.: Latest Attainments of the Study of the Highest Nervous Activity of Animals, Bull. de l'Inst. Scientifique Lesshaft **8**, 1924.

7. Panferov, J. K.: On Disturbance of the Balance Between Irritation and Inhibition with Children in Cases of Difficult Differentiation of Acoustic Rhythmical Stimulations. A report at a Physicians' Meeting in the Children's Clinic of the Medical Institute, March 15, 1925.

were more difficult, that is, between 144 and 108 beats of the metronome. This differentiation was also quickly accomplished by the child by means of five nonsupported irritations (104 beats). Then followed the experiment of bringing the active and inactive stimulators still nearer to each other, that is, 144 and 120 beats were applied. This differentiation was formed after four nonsupported irritations, but the condi-

TABLE 1.—*Findings for Four Months*

Date, 1924	No. of Stimulation	Time	Stimulation	Conditioned Reflex	Latent Period	Remarks
3/ 6	91	12:04	Metronome 144	+	0.4	Goes to the experiment quickly and laughing, gets into the apparatus by himself
	92	12:07	Metronome 144	+	0.5	
	93	12:13	Metronome 144	+	0.4	
	94	12:15	Metronome 144	+	0.5	
4/ 4	159	3:05	Metronome 144	+	1.2	A calm, well balanced and quiet child
	10	3:07	Metronome 92	0	—	
	160	3:09	Metronome 144	+	1.5	
	161	3:11	Metronome 144	+	1.0	
	11	3:14	Metronome 92	0	—	
	162	3:17	Metronome 144	+	1.3	
5/21	267	1:09	Metronome 144	+	0.9	After the experiment laughs and talks
	268	1:12	Metronome 144	+	0.9	
	6	1:15	Metronome 108	0	—	
	269	1:18	Metronome 144	+	...	
5/29	275	2:48	Metronome 144	+	1.2	
	7	2:51	Metronome 108	0	—	
	276	2:54	Metronome 144	+	0.7	
	277	2:57	Metronome 144	+	0.7	
	1	3:00	Metronome 120	+	2.0	
	278	3:03	Metronome 144	+	0.6	
5/31	280	2:01	Metronome 144	+	0.8	Refuses going to the experiment; walks and mounts slowly to the apparatus; after the experiment is silent
	281	2:04	Metronome 144	+	0.9	
	282	2:07	Metronome 144	+	0.8	
	283	2:12	Metronome 144	+	1.0	
6/ 8	321	12:38	Metronome 144	+	1.2	Goes to the experiment silently and gets into the apparatus; report from the ward of a change in the patient's behavior, he has become taciturn
	322	12:41	Metronome 144	+	0.7	
	4	12:44	Metronome 120	0	—	
	323	12:47	Metronome 144	+	1.0	
	324	12:50	Metronome 144	+	1.5	
	1	12:53	Metronome 132	+	1.7	
	325	12:56	Metronome 144	+	0.9	
6/18	330	12:40	Metronome 144	+	1.2	Is rude, fights with other children; insists on being discharged from hospital; doctor's report from the ward that his behavior is insupportable, he is extremely excited, fights and is disobedient
	6	12:43	Metronome 120	+	5.3	
	331	12:47	Metronome 144	+	2.0	
	2	12:50	Metronome 132	+	3.0	
	3	12:53	Metronome 132	+	2.0	
	332	12:56	Metronome 144	+	0.9	
6/22	348	1:04	Metronome 144	+	...	
	12	1:07	Metronome 132	+	1.1	
	13	1:10	Metronome 132	+	0.5	Yawns, is sleepy, closes his eyes; at 1:17 falls asleep for the first time after five months of experimenting; at 1:23 awakes from a knock at the door
	14	1:15	Metronome 132	+	1.4	
	349	1:25	Metronome 144	+	0.8	

tioned reflex activity of the child had changed. The latent periods of conditioned reflexes had increased in length twice (instead of 0.4 to 0.5 seconds it became 0.8 to 1.9 seconds; experiments performed on May 29 and 31). At the same time we observed an important change in the behavior of the child; having always been easy to deal with and quiet during the experiments, he now became irritable and refused to go to the laboratory.

Once more we made a differentiation which was still more difficult, that is, 144 and 132. During the work which now began, we were informed from the child's ward that the patient had become nervous; he had always been well behaved; now he cried often, beat the other children and said he wanted to leave the hospital. The experiments had to be discontinued, as not only no new differentiations could be formed, but even the differentiation of June 18 between 120 and 144 beats of the metronome had disappeared (experiment performed on June 18). The inactive stimulation of 132 beats began to cause yawning and sleepiness, and during the fourth stimulation the child went to sleep, which happened for the first time in the course of the whole work of five months (experiment performed on June 22, Table 1).

Thus, the more difficult the differentiation became, the more the balance between irritation and inhibition was disturbed; therefore the differentiating activity of the child lessened, a general inhibition developed during the experiment (sleep), while the whole behavior of the child was changed.

I observed the same facts with Dr. V. V. Syriatsky while studying on children the difficult differentiations on the skin. When we had formed too many active and inactive places on the child's skin, systematically accompanying by food the first and not the latter, the child became restless; it would refuse to come in for the experiments; the intensity of the conditioned reflexes and the exactness of local differentiations were diminished.

DELAYED REACTIONS

Some interesting facts were discovered by Dr. V. A. Haloutina-Zinserling [8] and me while studying the so-called "delayed" conditioned reflexes in children. These reflexes were formed in the following way: In forming the ordinary conditioned reflex, we gave the food a few seconds after the beginning of the action of the external agent; but here the feeding was more and more retarded. Under these circumstances, the motor reaction of the mouth was also delayed until the time of feeding. Now the external agent at the beginning of its action does not produce a conditioned reflex, but the latter takes place about the time when the unconditioned stimulus—feeding—begins to act.

The forming of these "delayed" reactions is based on the development of cortical inhibition and is one of the most difficult processes for the child. Being so difficult to form, these delayed reactions were of special interest to us.

A conditioned reflex from the metronome was formed in a child, N. S., aged 6, by giving food five seconds after the metronome had started. This reflex can be seen in Chart 1. When the reflex became

8. Haloutina-Zinserling, V. A.: The Study of Delayed Conditioned Reflexes with Children, Dissertation, 1925.

stable, we began to delay it. Instead of giving food five seconds after the metronome had started, we began to give it with the thirtieth second. After several such stimulations, the conditioned reflex lost its stability and rapidly disappeared. The child began to yawn and to be sleepy; the development of an intensive inhibition was the result of these experiments.

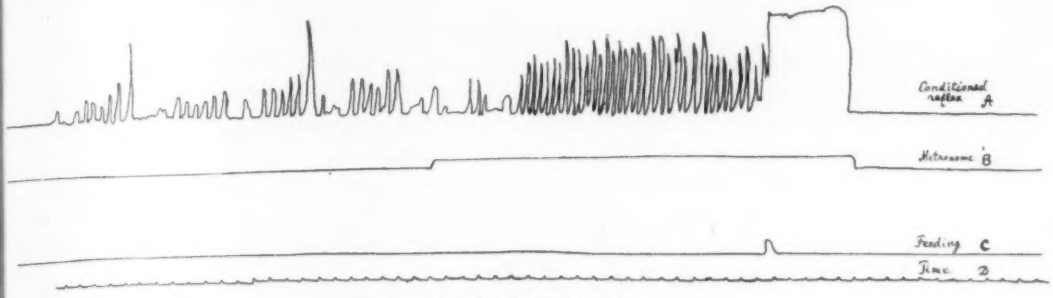


Chart 1.—Conditioned reflex in N. S.

Then we began to give food again five seconds after the starting of the metronome. Although for five days there was no reflex, for the next three days it was unstable, and not until the eighth day did it become as it had been.

Then we delayed the reflex again for thirty seconds. This time no general inhibition developed, but the reflex began to be removed. At

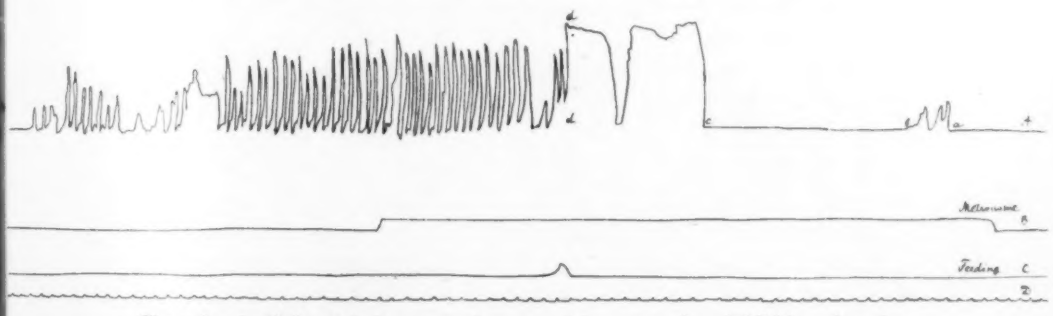


Chart 2.—A slight and short reaction, *a* and *b*; a complete inhibition, *b* and *c*; the fully developed conditioned reflex, *c* and *d*.

the beginning of conditioned stimulation there appeared a slight and short motion reaction (Chart 2, *a* and *b*); after that came a complete inhibition (*b* and *c*), and then the motor reaction reappeared near the moment of feeding, that is, twenty-two and two-tenths seconds after the metronome had been started.

We see that the inhibition at the beginning is not sufficient to inhibit the reflex, and the latter breaks through (*a* and *b*); however, after that

the inhibition is gradually augmented and inhibits the reflex completely (*b* and *c*); when it is nearer the feeding, it again relaxes, and we see the fully conditioned reflex (*c* and *d*).

When the delayed reflex had been stabilized the inhibition was strengthened, and, as is seen on Chart 3, there was no more wave *a* and *b* at the beginning, and the motor reaction corresponded to the moment of feeding.

When we had succeeded in delaying the reflex for thirty seconds, we made the conditions of the experiment still more difficult, that is, we began to delay the reflex for sixty seconds. After several such trials the reflex disappeared again; the child began to sleep during the experiments, and refused to go to the laboratory.

All experiments were discontinued for a week, and the child was given full rest. This rest had an excellent effect. When we renewed our work and tried to delay the reflex for sixty seconds, it did not disappear but became delayed for forty and six-tenths seconds (Chart 4); also there were no more difficulties in getting the child to go to the laboratory for the experiments.

Thus, as in the case of the differentiating process, so also in the case of forming delayed reactions, as soon as the conditions grew to be more difficult the balance failed and an intensive inhibition developed, which increased to the degree of sleep; at the same time the usual conditioned reflectory activity ceased. It took a whole week of training the reflexes the first time or giving full rest to the child the second in order to free the cerebral hemispheres from this inhibition and restore the normal balance.

The disturbance of the balance was still more apparent in our experiment with Dr. E. V. Minervina,[9] performed on an hysterical child.

S. G., a girl, aged 12, was taken to the Children's Clinic of the Medical Institute with symptoms of globus hystericus and frequent vomiting after the ingestion of food. A year before, the patient had drunk some anisated solution of ammonia by mistake, and after this she began to vomit. She was brought to a hospital, where, however, the physicians did not find any symptoms of poisoning. From that time the patient continued to vomit after eating, when excited. When the patient was excited on an empty stomach, dyspnea, cyanosis and twitching of the muscles of the face occurred, instead of vomiting. Thus the stimulation had two different effects: with a full stomach it radiated to the vomiting center, and with an empty stomach to the respiratory and circulatory centers.

9. Minervina, E. V.: On the Conditioned Reflectory Activity in Hysterical Children. A report read at a Meeting of Physicians of the Children's Clinic in the Medical Institute, April 2, 1925.

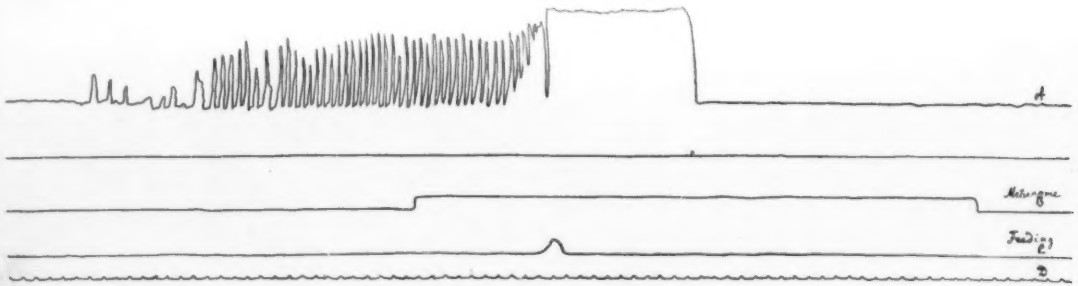


Chart 3.—Stabilized reflex.

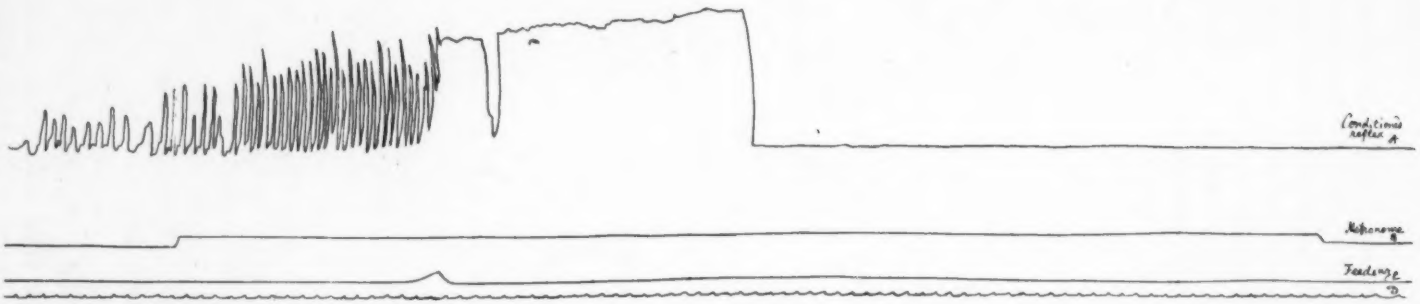


Chart 4.—The curve *a* registers the motory reaction of opening the mouth; *b*, the beginning and the end of the conditioned stimulation (metronome); *c*, themoment of feeding and *d*, the time in seconds.

When our patient was first brought to the laboratory, she exhibited an intensive passive-defensive reaction. Usually there is no difficulty in putting the children on the table for experiments, but in this case another child had to be called and placed in the apparatus, before she would lie down.

Then in five minutes we stimulated her by the beats of the metronome. This stimulation produced intensive excitement, which was expressed by dyspnea, cyanosis and convulsions of the muscles of the face. The second stimulation had the same result. The third stimulation caused a weaker reaction, and beginning with the fourth, one new fact was observed. The metronome from the first beats began to cause intense sleepiness in the child. As soon as the metronome began to act the patient closed her eyes, breathed heavily and held a biscuit between her teeth during the whole time of the action of the metronome. One or two minutes after the stimulation with the metronome, the sleepiness passed, and she began to eat the biscuit. Thus the metronome, which at first developed intensive stimulation, now caused inhibition. Two or three seconds after the beginning of its action the child was dazed by a strong, stable, widely radiating inhibition (experiment performed on January 18, Table 2).

Then, together with Professor Pavlov, we decided to make this inhibition conflict with intense excitement. We made the following experiment: we wanted to see what would happen if we applied the metronome, not when the child was having full rest and the innumerable impulses from muscles, ligaments, and articulations were minimal, but in conditions of extreme motor excitement, that is, in dancing. That was easy enough, as the patient thought that she could dance well.

For once we broke our rule of not entering into any conversation with the patient, and in this special case asked her to dance. She began to do so, and when she reached the greatest motor effect, the metronome was put in action. The patient stopped instantly; for a minute or so she stood bending her body slightly to and fro with her eyes fixed on one point; then dyspnea, tremor and cyanosis developed quickly, and she began to sob. When in ten minutes it was possible to put her back into her place, she ceased crying, lay quietly, but refused to take a biscuit. The experiment was interrupted (experiment performed on January 24, Table 2).

On the second day, the patient refused to go to the laboratory. The following day, she went, but, as before, showed a strong defensive reaction to the surroundings. However, she lay down in her place and was more or less quiet. As soon as the metronome was set in action she stopped her ears, her respiration became quicker, her face reddened and the muscles of her face twitched. When the metronome ceased she was quiet again. The same thing was observed every time the metro-

nome was started. During the next two days the metronome produced the same effect. On the third day, the reaction of excitement from the metronome gradually began to be less; it did not disappear until the sixth day. But now the metronome has lost its inhibitory power, which it developed so intensively before our experiment with the dance. Our patient did not sleep now, neither did she appear to become excited. We were able to form the conditioned reflex with this stimulator. The reflex was being formed extremely slowly. Only at the one hundred

TABLE 2.—*Results of Experiments*

Date, 1924	No. of Stimulation	Time	Stimulation	Conditioned Reflex	Feeding	Remarks
1/18	24	3:05	Metronome 138	Sleep	Feeding	Goes to sleep with the first beats of the metronome; in two minutes awakes and begins to chew
	25	3:09	Metronome 138	Sleep	Feeding	The metronome at once causes sleep; the biscuit sticks between the teeth; when the metronome stops, awakes gradually and eats the biscuit
1/24	36	1:10	Metronome 138	Sleep	Feeding	Sleeps at the fifth beat of the metronome; the biscuit is held by the lips; in two minutes opens her eyes and begins to eat
		1:16	.....	.....	.....	Being asked to dance an adagio she gets up slowly and smiles weakly
		1:17	.....	.....	.....	She dances two minutes
	37	1:19	Metronome 138 + dancing	.....	.....	Danced 15 seconds while the metronome was beating; stopped dancing abruptly; stood motionless in a pose; dyspnea, cyanosis, tremor; tears
	38	1:29	Metronome 138	.....	Feeding	Defensive reaction toward the metronome, tremor, tears
1/26	39	12:52	Metronome 138	.....	Feeding	At the sound of the metronome, stops her ears; dyspnea; tears; after the metronome has ceased becomes quiet gradually
	40	12:55	Metronome 138	.....	Feeding	Stops her ears to the metronome
	41	1:01	Metronome 138	.....	Feeding	Starts at the sound of the metronome; stops her ears; chews the biscuit very slowly
1/28	42	12:04	Metronome 138	.....	Feeding	Stops her ears to the metronome
	43	12:07	Metronome 138	.....	Feeding	Stops her ears

and forty-fifth trial did a slight reflex appear; for a long time it was very unstable, and only at the two hundred and ninety-fifth trial did it become constant. It is interesting that the further study of this reflex showed that it disappeared very slowly; about ten stimulations unaccompanied by food were necessary to cause the conditioned reflex to disappear. The reflex, which was formed with extreme difficulty, was also with difficulty inhibited.

From these experiments we see the difference between the reaction produced by external stimulation in a normal and in a pathologic child. The whole activity of the cerebral hemispheres in a normal child is

founded on a flexible balance between the irritative and inhibitory processes; here irritation and inhibition regularly and easily replace one another, depending on changing external circumstances. In our pathologic case this flexibility of the balance was lost. We could see that the metronome at first acted for a long time as an intensive inhibitory agent. After that, it produced extreme excitement for five days. Then for a certain time the balance was restored, and we could form the conditioned reflex. However, this reflex could be made to disappear with great difficulty, because now inhibition was lacking. Thus instead of a normal flexibility of the balance, inhibition (sleep) or extreme excitement prevails.

Our experiments show the consequences when intense stimulation conflicts with strong inhibition. An extended and great disturbance of the balance occurs even if such an elementary activity of the cortex as the formation of conditioned reflexes is obstructed. In life such conflicts always take place, but in the normal nervous system a disturbance of balance is quickly restored. However, it acquires a more serious character when several severe conflicts follow one another, or when the child's central nervous system itself shows some pathologic inborn deficiency.

With Dr. V. V. Dobrovolskaia,[10] I studied the constant disturbance of the balance in a patient after an attack of epidemic encephalitis.

J. V., a boy, aged 6, had epidemic encephalitis two years prior to examination. As a result he suffered from attacks of excitement and dyspnea, intensive salivation and motor excitement, during which he broke window panes, tore his clothes and destroyed any objects he could get at. These attacks occurred when he encountered any resistance. The child suffered from severe insomnia.

An examination of conditioned reflexes showed that in this case they were formed even sooner than in normal children. On the other hand, the inhibitory process was pathologically deficient, that is, the child formed the conditioned inhibition with great difficulty. We had to apply a tactile stimulation of the skin thirty times and use the metronome without feeding in order to form an inhibitory reflex from this stimulation. A normal child forms a conditioned inhibition after from two to six stimulations not seconded by an unconditioned reflex, that is, food (Dr. N. R. Shastin).[11]

While investigating inhibitory reflexes in the same child, some new and important facts were found. As had been shown by Dr. Shastin

10. Dobrovolskaia, V. V.: On Stable Disturbance of Reciprocal Relations of Irritation and Inhibition in Children. A report read at a Meeting of Physiologists at the Institute of Experimental Medicine, March 19, 1925.

11. Shastin, N. R.: On Conditioned Inhibition in Children. Dissertation. Voronesh, 1922.

at our laboratory, the accumulation of conditioned inhibitions in normal children causes a progressing inhibition, which assumes a general character and leads to the child's going to sleep. In our case we had just the opposite results. As soon as we began to repeat conditioned inhibitions, the accumulating of them produced excitement with dyspnea, cyanosis and salivation. This excitement increased progressively, and by the eighth inhibition had reached the point of making the child cry, scream and destroy the surrounding objects (Table 3). The excitement began to subside only when we applied a conditioned reflex, but we had to feed the child three times while he was listening to the beat of the metronome before he calmed down.

TABLE 3.—*Results of a Further Experiment*

Date, 1924	No. of Stimulation	Time	Stimulation	Conditioned Reflex	Latent Period	Remarks
4/11	357	12:36	Metronome 116	+	9.8	
	40	12:38	Metronome 116 + skin stimulation	0	—	The child is quiet
	41	12:41	Metronome 116 + skin stimulation	0	—	The child is quiet
	42	12:43	Metronome 116 + skin stimulation	0	—	The movements of the child increase
	43	12:45	Metronome 116 + skin stimulation	0	—	The number of respirations augment
	44	12:47	Metronome 116 + skin stimulation	0	—	The child begins to spit, knocks incessantly at the wall of the apparatus
	45	12:49	Metronome 116 + skin stimulation	0	—	Tries to throw off with his hand and leg the apparatus for skin stimulation on leg
	46	12:51	Metronome 116 + skin stimulation	0	—	Cyanosis, dyspnea
	47	12:53	Metronome 116 + skin stimulation	0	—	The child cries and screams
	358	12:55	Metronome 116	0	—	Cyanosis, dyspnea
	359	12:57	Metronome 116	0	—	Crying ceases
	360	12:59	Metronome 116	0	—	Dyspnea decreases
	361	1:01	Metronome 116	0	—	The child is calm again
	362	1:03	Metronome 116	+	2.0	

What has caused that strong excitement in this child?

As we know from Professor Pavlov's investigations on dogs, the cortical inhibition inducts irritation in other parts of the cerebral hemispheres—the so-called positive induction. This positive induction also occurs as a result of inhibitory reactions in children. However, inducted irritation in most cases remains strictly limited and produces no general excitement. In our pathologic case (investigations of Dr. Dobrovolskaia), the inhibition caused by the accumulating of several conditioned inhibitions caused an irritative process of such intensity that it radiated widely, not only over the cortex, but also over the lower parts of the central nervous system, causing dyspnea, cyanosis and salivation. In a lesser degree, the positive induction and subsequent wide radiation of irritation was observed in other neuropathic children in the form of defensive reaction, crying, etc. (affects).

However, as proved by the following experiments, the intensive excitement in our case was the result of continual repetition of inhibitory reflexes. It was interesting to learn the possibility of applying the same number of inhibitions without causing that general excitement. That was attained by fractional dosing of inhibition. We began to alternate conditioned inhibitions and conditioned reflexes. As shown in Table 4, in that case there was no general excitement.

Intense general excitement was also observed when applying difficult differentiations. When differentiating from 50 to 150 beats of the metronome, the child was quiet, while from 50 to 92 caused general excitement.

TABLE 4.—*Results Showing no General Excitement*

Date, 1924	No. of Stimulation	Time	Stimulation	Conditioned Reflex	Latent Period	Remarks
4/22	442	2:04	Metronome 116.....	+	2.1	The child is quiet
	87	2:07	Metronome + skin stimulation	0	—	The child is quiet
	88	2:08	Metronome + skin stimulation	0	—	
	443	2:09	Metronome 116.....	+	4.0	
	89	2:10	Metronome + skin stimulation	0	—	The child is quiet
	444	2:11	Metronome 116.....	+	2.7	
	90	2:13	Metronome + skin stimulation	0	—	Sings and smiles
	445	2:13	Metronome 116.....	+	4.0	
	91	2:14	Metronome + skin stimulation	0	—	
	92	2:15	Metronome + skin stimulation	0	—	
	446	2:16	Metronome 116.....	+	2.8	
	93	2:17	Metronome + skin stimulation	0	—	Whistles
	94	2:18	Metronome + skin stimulation	0	—	
	447	2:19	Metronome 116.....	+	1.9	
	95	2:20	Metronome + skin stimulation	0	—	
	448	2:21	Metronome 116.....	+	3.8	
	96	2:22	Metronome + skin stimulation	0	—	Is quiet
	449	2:23	Metronome 116.....	+	1.7	
	97	2:24	Metronome + skin stimulation	0	—	
	450	2:25	Metronome 116.....	+	1.4	
	98	2:26	Metronome + skin stimulation	0	—	Is quiet
	451	2:27	Metronome 116.....	+	3.7	
	99	2:28	Metronome + skin stimulation	0	—	
	452	2:29	Metronome 116.....	+	15.0	
	100	2:30	Metronome + skin stimulation	0	—	Is quiet
	453	2:31	Metronome 116.....	+	1.3	
	101	2:32	Metronome + skin stimulation	0	—	
	454	2:33	Metronome 116.....	+	1.7	

COMMENT

Our experiments have proved that the most intensive induction and radiation of irritation occur in cases of conditioned inhibition, in a lesser degree in those of differentiation and least of all in causing conditioned reflexes to disappear.

A constant disturbance of the balance toward irritation, due to a deep abatement and nonstability of the inhibitory process was the result of organic changes produced by epidemic encephalitis. The patient's nervous system was extremely irritable, being absolutely weakened in its inhibitory function.

Thus the normal highest nervous activity, the whole behavior of the child, is founded on the highly flexible balancing between irritation and inhibition.

The keeping of the balance in children and in animals sometimes requires great energy. Every limitation of irritation by inhibition, every formation of the antagonistic conditioned reflexes, produces some symptoms of general excitement or inhibition. The intensity of these symptoms depends on the power of the reflexes which are being inhibited. The more intense the stimulation is, the more difficult it is for the organism to limit and inhibit it. Sometimes the mobilization of all resources of the nervous system of the child are needed in order to suppress a reflex of great power.

The personality of the child also plays a great part. In some neuropathic children we observed the symptoms of extreme excitement, that is, restlessness, active defensive reaction, crying, while in others, on the contrary, we observed a general inhibition with the complete disappearance of conditioned reflexes and even with the development of a deep sleep.

The disturbances of the balance in pathologic children have, as a rule, a more lasting and profound character than in normal children.

The intensive conflicts between irritation and inhibition form a favorable soil for the origin of different neuroses in childhood. We know how serious neuroses can develop as a result of such catastrophic collisions in consequence of inhibiting the powerful sexual reflex in adults. We have just been observing a child, N. N., aged 8 years, with whom a complete displacement of the balance toward inhibition and an entire change of the whole behavior developed after an attempt to violate her had occurred. Thus, the intensive conflicts between stimuli and inhibition in children sometimes produce a disturbance of the balance which influences the whole behavior of the child and is the cause of the development of serious neuroses. This is the origin of most neuroses in children.

TREATMENT

Both physicians and teachers must endeavor to strengthen and train the child in forming inhibitory reflexes and in limiting irritation by inhibition from its earliest age, because all discipline and education is an uninterrupted limitation of reaction by inhibition. On the other hand, they have to guard carefully the weak, developing nervous system from the catastrophic conflicts of irritation and inhibition. In trying to limit the reaction, the physician and teacher should in each case thoroughly consider individual inhibitory power of the child and the intensity of the reflex which they want to inhibit. Doubtless the frequent neuroses in the family and at school are due to an insufficient appreciation of these two items.

The physician cannot properly treat a neurosis in a child unless he finds out what conflicts caused that neurosis; he must first remove the

cause. In our cases the experiment itself contained the conflict; therefore our treatment consisted in giving the children complete rest (with no experiments). That was generally sufficient to restore the balance. Sometimes we also gave bromids. According to the investigations of Dr. Petrova and Dr. E. M. Kreps at the laboratory of Professor Pavlov, bromids intensify not only the inhibition but also the irritation, that is, they are a good regulator of the activity of the cerebral hemispheres. However, the regulating effect of bromids could be noted only when there were functional disturbances of the balance. The application of these two methods gave excellent results in our cases, in which there were no serious organic changes.

DRIED HUMAN MILK

IV. DRIED HUMAN MILK AS A FOOD FOR INFANTS *

PAUL W. EMERSON, M.D.
BOSTON

In 1920,[1] on the Boston Floating Hospital, we began the preservation of dried human milk. An account has been given elsewhere of the development of the machine for drying human milk,[2] and of the feeding of the milk to animals.[3]

In 1922, the first year that we fed dried human milk to infants, we had only a small amount on hand, and the condition of the milk after drying was not so satisfactory as it was later. However, we found that human milk in this form was acceptable to babies as a food. Whether they would lose, maintain their weight or gain, we tried to find out in 1923, when we fed seven babies with dried human milk. Because of the newness of this food, we had to feed the babies very carefully, and, as a result, at first rather underfed them. The analysis of the dried product was compared with an analysis of the same milk in the fresh state, and showed very little loss by the process of drying; the formula for dried human milk is 32 per cent. fat; 65 per cent. carbohydrates; 12 per cent. protein. In its dried form the volume is approximately one-tenth of the original fresh milk.

The cases can be considered as a whole to advantage. All of the family histories were negative; all of the babies were full term. There was a question of cerebral injury in one. All of the babies weighed 6 pounds or more at birth; the largest weighed 9½ pounds. Six weeks was the longest that any of them had been breast fed. One infant was never breast fed. One baby refused to nurse, and, on an attempt to make him take the breast, under the orders of the local physician, the infant lost 2 pounds 6 ounces in four weeks, his weight falling to 5 pounds, 10 ounces.

On admission, all of these infants were at or below their birth weight, except one who weighed 2 pounds over at the age of 9 months. Six of the nine were 3 months of age, one was over 3 months and 2 were under three months. Seven of the nine were regurgitating or vomiting, and three of the nine had loose stools. Six out of nine had been fed on one or more proprietary foods. One baby was hypertonic;

* Received for publication, Sept. 26, 1925.

* From the Boston Floating Hospital.

1. Emerson, P. W.: The Collection and the Preservation of Human Milk. Preliminary Report, J. A. M. A. **78**:64 (March 4) 1922.

2. Smith, L. W., and Emerson, P. W.: Notes on the Experimental Production of Dried Breast Milk, Boston M. & S. J. **191**:938 (Nov. 13) 1924.

3. Smith, L. W.: The Experimental Feeding of Dried Breast Milk, J. Biol. Chem. **61**:625 (Oct.) 1924.

one had an elongated uvula which was found retroverted into the nasopharynx. All of the infants were in poor condition; one had a temperature of 96 F. plus, and received the same treatment as a premature child. Another was cyanotic and was put at once on the dangerously ill list. Another had spent the previous six weeks in an eye and ear hospital, owing to a purulent inflammation of the eyes. Two infants had inguinal hernia; one had a slightly cleft palate. Four of the nine infants had rickets. There was one case of pyelitis, and that in a boy, but four infants showed ten or more pus cells to a high power field on at least one examination. One baby had thrush. In six children the red blood count was under 4,600,000, the lowest being 3,600,000. The hemoglobin was 50, 65 and 70 per cent. in three cases, and in three others it was 80 per cent. (Tallquist). All of the Wassermann and Pirquet tests, and all of the Schick tests except one, were negative.

We have here, then, a group of infants in poor condition with histories of vomiting, loose stools and failure to gain, with a possible cause for the vomiting in three cases; namely, a cerebral injury, a hypertonia and an elongated uvula. All of these infants were not given dried human milk at the very beginning, but were placed on dilutions of cows' milk, sweet or acid, for from two to seven days.

PROCEDURE

The procedure in feeding the babies differed in 1922 and 1923, and it will be better to consider these cases separately from now on. In 1922, two babies were fed on dried human milk for thirty-four and forty days, respectively, the age of the oldest milk ranging from twenty-one to twenty-nine days. One infant was fed for a time on dried human milk; he was changed to fresh human milk, and then to a mixture of fresh human milk fat and cows' skim milk.

At that time we were not certain that dried human milk could be saved for a long time without becoming rancid. We now have milk that was dried five years ago and some of which was fed to guinea-pigs this year with subsequent gain. But in the event that the whole human milk would not keep, skimmed or centrifugalized human milk might be kept because of the elimination of fat. Skimmed human milk might conceivably be of great value in vomiting infants with intoxication, and we intend to try this form of feeding with the dried milk this summer. It would still leave the problem of how we were to save the cream. One way to dispose of it would be to feed it, along with cows' skim milk, preferably to patients with fat intolerance, and it was to see what value it might have as a food that we tried it on the first of these two cases.

The foods are arranged in Table 1 not as they were fed, but in order of the number of grams gained while on the food. It will be seen how

little gain was made on dried human milk alone. The best gain, of course, was made on fresh human milk. Dried human milk in the second line is grouped with cows' milk diluted, because we shifted gradually from one to the other, and on several days the baby was receiving both kinds of milk. It will be observed that the baby gained very well, comparatively, on human milk fat and cows' skim milk. Possibly there is room for this combination as a food if the fat can be preserved; lately we have been adding 50 per cent. cane sugar to the human milk fat, and boiling the milk down to make condensed milk. Our results with this form of preserved milk will be given in a later communication. The breast fat does not dry well.

The second baby did better, we think, on dried human milk, because on the average he was fed higher caloric and protein values throughout the summer.

TABLE 1.—*Weight Gained on Different Milks*

	Gain, Gm.	Time, Days	Protein per Kg.	Calories per Kg.
Fresh human milk	146	4	4.1	165
Dried human milk and cows' milk diluted	141	12	4.5	180
Whole cows' milk diluted	127	11	4.7	145
Human milk fat and cows' skim milk	114	12	3.7	180
Dried human milk	33	23	3.5	170

TABLE 2.—*Weight Gained on Different Milks*

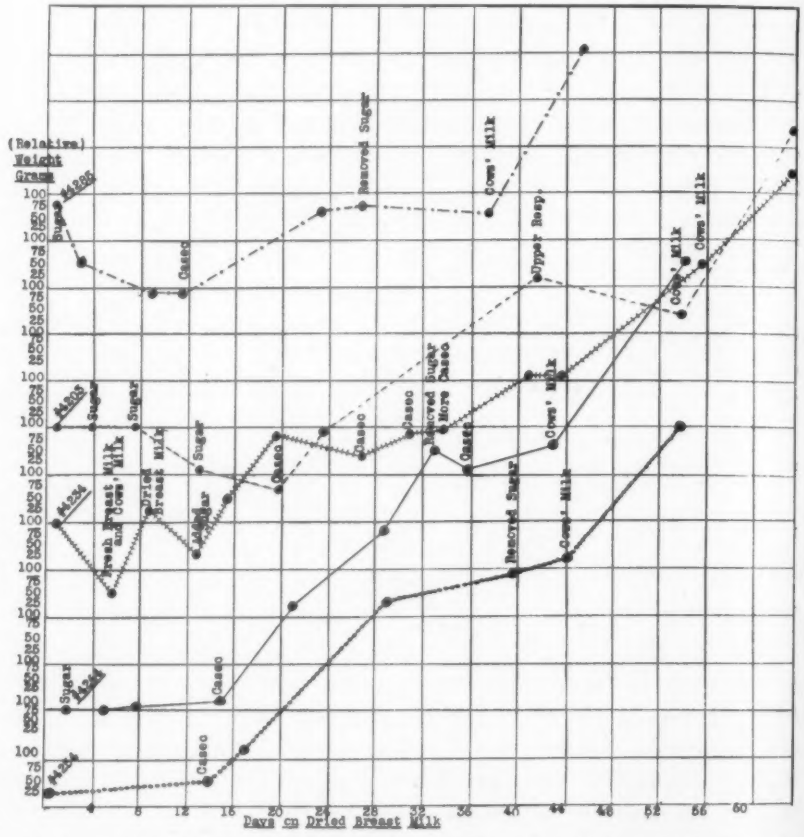
	Gain, Gm.	Time, Days	Protein per Kg.	Calories per Kg.
Fresh human milk	383	13	4	170
Dried human milk	148	37	3	140
Fresh human milk and cows' milk diluted	42	13	3.9	135
Cows' milk diluted	—28	7	3.9	85

In 1923, the procedure in feeding the infants was different. We started some of the babies on half-strength dried human milk and some on full-strength, but we found that a loss of weight occurred immediately; the calories and protein per kilogram both being low, namely, 108 and 1.8. We were unwilling to feed too high a fat content, and that there was much fat was evident in the stools and in the appearance of the milk. We, therefore, first added sugar in the form of lactose or dextrimaltose to increase the calories; later calcium caseinate was added to increase the protein content. Finally, we took out the sugar, keeping the caloric value nearly the same.

The longest time any baby was kept on the dried food was fifty-seven days; the shortest, sixteen days. Seven patients were fed for thirty-four or more days. The average age of the dried human milk was 100 days; the oldest, 120 days; in all of the infants, the milk fed was more than seventy-nine days old. All of the children were fed a mixture of cod liver oil and phosphorus, although one did not get it until

late in the season, and all of them were fed from 8 to 50 c.c. of orange juice daily. None of the infants developed the tenderness of scurvy. No roentgenograms were taken at the end of the season to detect the presence of active rickets.

When sugar was added to the dried human milk, making the sugar content in some cases as high as from 8.5 to 9.5 or 10.5 per cent., the result was a great increase in calories but no gain in weight. When



A chart which shows, first, the marked increase in weight subsequent to the addition of a brand of calcium caseinate to dried human milk already fortified by sugar and second, the increase in weight which followed the substitution of dried human milk by fresh cows' milk.

calcium caseinate was added, in from 1 to 1.5 or 2.5 per cent., to a food already high in calories but low in protein, there was an immediate response. The gain in weight was so marked in some patients that at first we suspected that some amino-acid, present in human milk in the fresh form, had been lost in the dried form and that it was this factor and not an increase in the protein which was responsible for the immediate

gain. On going over the percentages, however, we saw that the protein intake had been altogether too small to expect a gain on any food and that when a gain occurred, it was simply because there were enough calories and enough protein.

A glance at the chart will show that in each case, after calcium caseinate was added, there was a gain, but this was not due to the calcium caseinate alone; the food otherwise was high in caloric value from the addition of sugar, as has been pointed out; at the end of the season, the calcium caseinate was retained and the food was kept at or near its caloric value without the added sugar. This stage was not as conclusive as was hoped. Two of the children had upper respiratory infections just before the change was made, and in one the calories were reduced too much to permit a gain. In only one infant in whom the calories were kept up without the added lactose, did the child continue to gain; but here, the protein content was 8.8 gm. per kilogram of body weight. The question, whether the infants would gain by adding calcium caseinate alone, remained unanswered.

TABLE 3.—*Gain in Weight in Five Infants*

	Dried Human Milk		Cows' Milk	
Case	Gain, Gm.	Time, Days	Gain, Gm.	Time, Days
1	96	36	340	8
2	304	67	300	9
3	480	63	180	8
4	485	41	390	11
5	508	45	280	9

After taking the patients off the dried human milk gradually, it was observed that on cows' milk, diluted, there was a remarkable gain in a short time (Table 3 and the chart). This happened in each case, with too little change in the calories and protein to account for such a big gain. The question arose as to whether there were as many calories in the dried human milk as we thought there were.

Two patients are not in Table 3 nor in the chart, as one had neither calories nor protein enough to gain on any food, and the other was an older infant who vomited on any food offered him.

CONCLUSIONS

Human milk, in dried form, with an average age of 100 days, has been acceptable to a small group of babies as a food. Dried human milk has been fed to this group over an average time of thirty-four days. A small number of poorly nourished babies, fed on dried human milk, fortified with sugar, gained rapidly in weight, only after the addition of protein.

After being taken off dried human milk, the babies gained well on a cows' milk formula. This may have been due to the increased amount of protein.

COMPARATIVE SUGAR CONTENT OF BLOOD AND OF CEREBROSPINAL FLUID IN VARIOUS CONDITIONS *

A LEVINSON, M.D.
CHICAGO

It has been known for several decades that there is a reducing substance in the cerebrospinal fluid. At first, there was a question whether the reducing substance was glucose or pyrocatechin. Now, however, the presence of glucose in cerebrospinal fluid is beyond doubt, most workers agreeing with Schloss and Schroeder [1] that "the reducing substance in cerebrospinal fluid is a fermentable, dextrorotatory sugar, probably dextrose."

The amount of sugar in normal cerebrospinal fluid was found by the older authors to vary between 36 and 148 mg. per hundred cubic centimeters of fluid. More recent studies place the amount of sugar in cerebrospinal fluid between 40 to 75 mg. per hundred cubic centimeters of fluid.

Of late, some comparative studies have been made on the sugar contents of blood and cerebrospinal fluid under normal conditions and in cases of encephalitis. Special mention should be made of the work of Seham and Nixon,[2] Thalhimer and Updegraff [3] and Halliday [4] in human cerebrospinal fluid and Ino [5] in the cerebrospinal fluid of rabbits.

A good deal of data exist on the amount of sugar in cerebrospinal fluid in cases of meningitis. Comparatively little work, however, has been done on the relation of sugar in cerebrospinal fluid to that of the blood in various forms of meningitis. So far as we know, there are three references in the literature on that subject, namely, the work of

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* Received for publication, July 24, 1925.

* From the Sarah Morris Hospital for Children of the Michael Reese Hospital, and the Nelson Morris Memorial Institute for Medical Research.

1. Schloss, O. M., and Schroeder, J. C.: Nature and Quantitative Determination of Reducing Substance in Normal and Pathologic Cerebrospinal Fluid, Am. J. Dis. Child. **11**:1 (Jan.) 1916.

2. Seham, G., and Nixon, C. E.: Comparative Studies in the Chemistry of Blood and Cerebrospinal Fluid, Arch. Int. Med. **28**:561 (Nov.) 1921.

3. Thalhimer, W., and Updegraff, H.: The Sugar Content of the Blood and Spinal Fluid in Epidemic Encephalitis, Arch. Neurol. & Psychiat. **8**:15 (July) 1922.

4. Halliday: The Spinal Fluid Sugar in Encephalitis, Quart. J. Med. **18**: 300, 1925.

5. Ino: Acta Scholae Medicinalis, Univ. Kiota, No. 4, 1920-1923, 609, quoted by Goodwin and Shelley.

Hopkins,[6] of Wilcox and Lyttle [7] and the recent study of Goodwin and Shelley.[8]

Of particular interest in this study was the comparative content of sugar in blood and cerebrospinal fluid in cases of meningitis. It was also interesting to determine the effect of the injection or ingestion of glucose on the cerebrospinal fluid sugar.

METHOD

In most cases the cerebrospinal fluid was obtained twelve hours after the patient had any food, in order to avoid an increase in cerebrospinal fluid sugar due to ingestion of carbohydrates. In a few cases, fluid had to be withdrawn before the twelve hour period was up in order to settle the diagnosis or to institute treatment. In no case, however, did the patient get any food three hours prior to the removal of fluid.

With the exception of one case of encephalitis, in which the fluid was removed by means of ventricular puncture, all fluid was obtained by means of spinal puncture.

When glucose was given, it was introduced intravenously or intraspinally, with the exception of one case of encephalitis in which the glucose was given by gavage.

The Folin-Wu method [9] was used for the determination of sugar, both in blood and cerebrospinal fluid. For blood, the original method was followed in all its details. For cerebrospinal fluid, the following modifications were employed:

For nonmeningitic cerebrospinal fluid, we used 2 c.c. of fluid, 1 c.c. of tungstate, 1 c.c. of sulphuric acid and 6 c.c. of water, making a dilution of 1 to 5. For fluid suspected to be meningitic in character, when the sugar was expected to be markedly decreased, we used a dilution of 1 to 2.5; 1 to 1.25, and 1 to 0.625, in the latter case using only cerebrospinal fluid and the precipitating agent.

RESULTS

Our work bears out the results of previous workers in regard to the sugar content of cerebrospinal fluid. The sugar in our nonmeningitic cases varied between 46 and 76 mg. per hundred cubic centimeters

6. Hopkins: The Sugar Content of Spinal Fluid in Meningitis and Other Diseases, Am. J. M. Sc. **150**:847, 1915.

7. Wilcox, H. B., and Lyttle, J. D.: The Diagnostic Value of Sugar Concentration in Spinal Fluid, Arch. Pediat. **40**:215 (April) 1923.

8. Goodwin, G. M., and Shelley, H. J.: The Sugar Content of the Cerebrospinal Fluid and Its Relation to the Blood Sugar, Arch. Int. Med. **35**:242 (Feb.) 1925.

9. Folin, O., and Wu, H.: A System of Blood Analysis, J. Biol. Chem. **38**: 81 (May) 1919.

(Table 1). The lowest figure (46 mg.) was obtained in the fluid from a patient with brain abscess. There is a possibility, however, that there was a localized meningitis in connection with the brain abscess, as there were marked symptoms of meningeal irritation on that day and the fluid on the same day was turbid and contained many cells. Early in the disease as well as after the patient was operated on, with the consequent disappearance of the meningeal symptoms, the sugar contents of the cerebrospinal fluid ranged between 50 and 74 mg.

The amount of sugar in the cerebrospinal fluid bore no relation to the blood sugar. For instance, in a case of tetany with a blood sugar of 174 mg., the cerebrospinal fluid sugar was only 61 mg., or 35 per cent. of the blood sugar, and in a case of trichinosis with a blood sugar of 78 mg. the cerebrospinal fluid sugar was 60 mg., or 75 per cent. of the blood sugar. This would speak against the contention of Goodwin and Shelley [8] "that there is a definite relationship between the cerebro-

TABLE 1.—*Amount of Sugar in Blood and Cerebrospinal Fluid in Nonmeningitic Patients*

Name	Diagnosis	Blood Sugar, Mg. per 100 C.c.	Cerebrospinal Fluid Sugar, Mg. per 100 C.c.	Percentage Relationship of Cerebrospinal Sugar to Blood Sugar
B. G.	Acidosis	110	67	61
L. N.	Endocarditis	102	66	64
F. J.	Trichinosis	78	60	75
M. W.	Poliomyelitis	100	50	50
L. C.	Encephalitis	105	69	66
		120	76	63
		91	57	63
P. T.	Tetany	174	61	35
H. C.	Brain abscess	114	73	64
		90	46	51
		97	50	51
		115	74	65

spinal fluid sugar and the blood sugar, and that the figure representing this relationship, stated as the percental relationship between the two, is relatively constant, lying between 45 and 65 per cent., provided determinations are made on both blood and cerebrospinal fluid taken at the same time, after a night's fasting." This would also speak against the statement of Wilcox and Lyttle,[7] that "normally the spinal fluid sugar concentration is about one-half that of the blood, and that its range of variation corresponds to that of the blood."

In the cerebrospinal fluid of all forms of meningitis, sugar was markedly decreased, and ranged from a mere trace to 45 mg. per hundred cubic centimeters (Table 2). One case of meningococcus meningitis constituted an exception to the rule. Although the fluid was turbid, the sugar in the fluid was 95 mg. per hundred cubic centimeters. Possibly the fact that the fluid was removed as early as twelve hours after the onset of the disease may account for the high sugar content.

The blood sugar in various forms of meningitis was not uniform, being very high in some cases and low in others. Unlike the cerebrospinal fluid sugar, which was consistently low, the blood sugar varied in amount from day to day.

EFFECT OF INJECTION OF GLUCOSE ON CEREBROSPINAL FLUID SUGAR

In Ino's [5] experiments on rabbits, the cerebrospinal fluid sugar reached its maximum one hour after the injection of glucose and then required four hours to return to normal.

In Goodwin and Shelley's [8] experiments on human beings, the maximum rise in cerebrospinal fluid sugar after the injection of glucose was reached at the end of four hours, with the return to normal at the end of six hours.

TABLE 2.—*Amount of Sugar in Blood and Cerebrospinal Fluid in Various Meningitides*

Name	Diagnosis	Blood Sugar, Mg. per 100 C.c.	Cerebrospinal Fluid Sugar, Mg. per 100 C.c.	Percentage Relationship of Cerebrospinal Fluid Sugar to Blood Sugar
S. J.	Tuberculous meningitis	120	14	12
		97	14	14
J. W.	Tuberculous meningitis	112	22	20
		112	27	24
E. G.	Tuberculous meningitis	112	28	25
H. S.	Tuberculous meningitis	94	11	12
		116	12	10
A. R.	Tuberculous meningitis	115	35	30
M. T.	Tuberculous meningitis	145	34	23
L. G.	Tuberculous meningitis	149	45	30
I. W.	Tuberculous meningitis	94	19	20
D. R.	Tuberculous meningitis*	99	16	16
J. T.	Tuberculous meningitis	102	29	28
L. L.	Meningococcus meningitis	176	95	54*
		100	25	25†
J. R.	Streptococcus meningitis	157	Trace	..
G. W.	Influenza meningitis	84	26	31

* Twelve hours after onset, fluid turbid.
† After 150 c.c. serum.

Halliday found that the highest reading for cerebrospinal fluid sugar was obtained when the blood sugar had returned to the fasting level. He also found that the actual rise in cerebrospinal fluid sugar was a small one, the highest being an increase of 0.033 per cent. in three and one-fourth hours.

In our work, most of which was carried out before the publication of the before-mentioned observers, the cerebrospinal fluid in one case of encephalitis showed an insignificant rise in its sugar content (1 mg.) in one hour, a slightly larger rise (3 mg.) in two hours after the injection of glucose and a still greater rise in three hours (11 mg.). At another experiment, the same case showed a rise of 11 mg. two and one-half hours after injection of glucose, in spite of the fact that the amount of glucose injected was less than in the first experiment.

Blood sugar in the foregoing case of encephalitis was greatly increased one hour after injection of glucose and came down to normal in two hours. At another time, the blood sugar was still greatly increased two and one-fourth hours after injection of glucose.

In our experiments with tuberculous meningitis, there was a rise of 4 mg. of glucose in the cerebrospinal fluid one hour after injection. In another case, there was a rise of 7 mg. one hour after injection. In one case, there was a marked rise in the cerebrospinal fluid sugar in two and one-half hours (34 mg.). In another case, the cerebrospinal fluid sugar was practically at the pre-injection level. The same variation was true three hours after the injection of glucose. In one case, there was an increase of 70 mg. three hours later, and in another case, the sugar was practically at the pre-injection level.

TABLE 3.—*Effect of Glucose on Sugar in Blood and Cerebrospinal Fluid*

Name	Date	Diagnosis	Glucose	Blood Sugar, Mg. per 100 C.c.	Cerebrospinal Fluid Sugar, Mg. per 100 C.c.	Percentage Relation of Cerebrospinal Sugar to Blood Sugar	Amounts of Glucose Injected, Gm.
L. C.	7/ 3/24	Encephalitis.....	Before.....	105	69	66	7.5
			2½ hours...	132	80	61	
L. C.	10/ 4/24	Encephalitis.....	Before.....	91	57	63	12
			1 hour.....	143	56	41	
			2 hours.....	92	60	65	
			3 hours.....	60	65	108	
S. J.	5/28/24	Tuberculous meningitis	Before.....	108	14	13	12
			1 hour.....	138	18	13	
	6/ 2/24	.....	Before.....	110	14	13	12
			1 hour.....	198	21	11	
			2½ hours...	98	16	17	
H. S.	7/15/24	Tuberculous meningitis	Before.....	116	12	10	9
			3 hours.....	214	82	39	
I. W.	6/25/24	Tuberculous meningitis	Before.....	94	19	22	12
			3 hours.....	100	20	20	
D. R.	6/25/24	Tuberculous meningitis	Before.....	99	16	16	24
			2½ hours...	98	50	51	
J. T.	6/25/24	Tuberculous meningitis	Before.....	102	29	28	12
			2¾ hours...	226	84	36	
G. W.	8/ 1/24	Influenza meningitis....	Before.....	69	Trace	..	15
			Postmortem 2 hours.....	71	Trace	..	

It is evident from these results that the injection or ingestion of glucose increases the cerebrospinal sugar, but that no time can be set for the period of the maximum increase. In most cases studied, the greatest increase was between two to three hours after the injection of glucose both in meningitic and in nonmeningitic cases. In some cases, however, there was either no increase in the sugar or the maximum sugar curve was reached before the three hour period was up.

The usual increase in cerebrospinal fluid sugar on injection or ingestion of glucose would speak for the inadvisability of performing spinal puncture when cerebrospinal fluid sugar determination may be of value, one to three hours after ingestion of glucose or after any meal, which

contains carbohydrates. If the patient is not acutely ill, it is best to do the spinal puncture in the morning, after a night's fast. However, if the delay of the spinal puncture may delay the injection of serum or otherwise interfere with either the diagnosis or treatment, the food factor may be discarded.

We see no special advantage in the determination of blood sugar along with cerebrospinal fluid sugar, as in our cases there was no constant relation between the sugar in the blood and the cerebrospinal fluid.

CONCLUSIONS

1. The cerebrospinal fluid sugar in our series of nonmeningitic fluids varied between 46 and 76 mg. per hundred cubic centimeters of fluid. The lowest figure (46 mg.) was obtained in a case of brain abscess, with a turbid fluid containing many leukocytes. The next lowest figure was 50 mg. per hundred cubic centimeters.

2. The cerebrospinal fluid sugar varied from day to day.

3. The cerebrospinal fluid sugar bore no direct relation to the blood sugar.

4. The cerebrospinal fluid sugar in all forms of meningitis was low, varying from 45 mg. to a mere trace. In one case of meningococcus meningitis the sugar was unusually high a few hours after onset, but came down to 25 mg. in less than twenty-four hours.

5. The blood sugar in our cases of meningitis varied between 84 to 176 mg. per hundred cubic centimeters.

6. The sugar in the cerebrospinal fluid in a case of encephalitis showed an insignificant rise one hour after injection of glucose and a rise of 8 mg. three hours after the injection of glucose. Another time, it showed a rise of 11 mg. in two and one-half hours.

7. There was a rise of from 4 to 7 mg. in the cerebrospinal fluid sugar in a case of tuberculous meningitis one hour after the injection of glucose. In one case, there was a marked rise in the cerebrospinal fluid sugar two and one-half hours after injection (34 mg.). In another case, the cerebrospinal fluid sugar was practically at the pre-injection level. The same variation was true three hours after the injection of glucose.

8. Whenever possible, the sugar in cerebrospinal fluid should be determined on a specimen obtained several hours before the ingestion of food to exclude the possibility of error due to carbohydrate ingestion.

9. For clinical purposes, there is no special advantage in determining blood sugar along with cerebrospinal fluid sugar.

EXPERIMENTAL STUDIES ON RICKETS

III. PROTEIN SUBSTANCES AS A FACTOR IN NORMAL OSTEOGENESIS AND IN THE HEALING OF RICKETS *

ANDOR DE BOSÁNYI, M.D.
Associate Professor of Pediatrics, of the Children's Clinic, University Pázmány Peter, Budapest, Hungary
BALTIMORE

In two recently published papers, experimental studies on rickets were described, which indicated that a hitherto unknown relation exists between an unappreciated function of the bone marrow and the processes of calcification and ossification. These studies would seem to show that the marrow produces an organic substance which is essential for normal bone formation. The foregoing conclusion could be drawn from the fact that bone marrow given by mouth, or extracts of healthy bone marrow given hypodermically, induced healing in the bones of rats with rickets. No such effects were obtained from the marrow of rachitic bones. From these experiments it is obvious that the formation of normal bone is closely connected with a normal organic function of the bone marrow, and that the disorders of calcification and ossification in rickets may be closely connected with, or due to, pathologic changes in bone marrow function. These changes are most probably of the nature of a hypofunction, so that the rachitic marrow does not form the substance which normally plays a rôle in bone formation. Histologic changes have been observed in rachitic bone marrow which harmonize with the results of the before-mentioned physiologic observation. Marfan,[1] Hutinel and Tixier,[2] as well as Benjamin and Aschenheim,[3] have hypothecated such a function for the bone marrow, but their hypotheses were unsupported by experimental proof. These authors believed that the pathologic alteration in the physiology of the marrow was in the nature of a hyperfunction rather than of a hypofunction. No other investigators have regarded at all the significance of the marrow in the physiology of bone formation. My experiments emphasize the importance of a belief which I have long held that the bone is to be regarded as a physiologic unit—an organ system consisting of several kinds of tissues—and that the

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* From the Department of Chemical Hygiene, School of Hygiene and Public Health, Johns Hopkins University.

1. Marfan: J. de Path. et Physiol. Gen. 1909.
2. Hutinel and Tixier: J. de Path. et Physiol. Gen. 1909.
3. Benjamin and Aschenheim: Ergebn. d. inn. Med. u. Kinderh. **8**.

growth of bone, that is, the formation of new bone, is dependent on an interaction of the functions of all these tissues. It is common knowledge that another function of the bone marrow, namely, hematopoesis, is also deranged in rickets. The majority of clinicians and investigators who have studied this disease are wont to regard the anemia which is always present in the rachitic child as a secondary one, and only Heubner [4] and Marfan [1] have admitted the possibility of the primary nature of this disorder. I have always found a well-marked anemia in rats which had been eating McCollum's [5] rickets-producing diet No. 3143, and in many of the animals the anemia was always present in the third week of feeding the experimental diet. During the experiments reported in this paper, I have examined forty rats of different lots and have found that the anemia is, in a certain degree, proportional to the rachitic changes of the bones. Animals with healing, or with chronic rickets, never have such low percentages of hemoglobin as are found in rats in the acute stage of the disease. The difference was especially well-marked in rats given a rickets-producing diet (3897) which contained 4 instead of 3 per cent. of calcium carbonate. The rickets produced by this diet is not so severe as that which develops as a result of feeding the diet containing 3 per cent. of calcium carbonate. The rachitic metaphysis is not so broad, and spontaneous healing, as evidenced by irregular deposits of lime salts in the metaphysis, is of common occurrence. The anemia in these animals is never of so severe a grade as the anemia of rats fed on the original diet No. 3143, in which the rickets is severe and sometimes even exaggerated.

In this table, two groups of rats are compared, and it may be seen that rats with mild rickets show moderate grades of anemia, whereas in rats showing well marked rachitic changes the anemia is always more severe. The table shows, moreover, that in fourteen days an improvement takes place in the anemia in cases of spontaneous healing or healing produced by any antirachitic treatment.

It is legitimate to conclude that if one function of an organ has suffered a pathologic change as the result of disease, other functional changes may be brought about by the same condition. If all the beforementioned results, together with those which I have reported previously, are taken into consideration, the conclusion seems to be justified that a concurrent dysfunction affecting the production of a substance which is significant in ossification and calcification may occur, together with the well-known dyshematopoiesis of rickets. It is, however, a simple matter

4. Heubner: Lehrbuch d. Kinderh.

5. McCollum, E. V.; Simmonds, N.; Becker, J., and Shipley, P. G.: J. Biol. Chem. **53**:292 (Aug.) 1922.

to ascertain the nature of the relationship between the two functions of the marrow. In the experiments reported in this paper, I have endeavored to show whether hematopoiesis and dyshematopoiesis are related directly or indirectly to the process of ossification. In these experiments, an attempt has been made to discover whether the hemoglobin in rickets undergoes a qualitative or structural change, as it does a quantitative one, which would in any way affect the ossification of the bone.

Evidence has been obtained that the antirachitic factor in the healthy bone marrow of rats is a water-soluble protein. Water extracts of marrow contain a small amount of hemoglobin, about 1 per cent. as a rule. In view of this fact it became necessary to find out whether this hemo-

TABLE 1.—*Comparison of Two Groups of Rats*

No. of Lot and Rat	Diet	Addition	Days on Diet: Without Addition	Days on Diet: With Addition	Necropsy Findings	Hemoglobin Percentage
265/1	3897	.....	40	..	Mild rickets, little spontaneous healing	88
265/2	3897	.....	40	..	Mild rickets, little spontaneous healing	82
263/1	3897	.....	58	..	Mild rickets, more advanced healing	92
263/2	3897	.....	58	..	Mild rickets, more advanced healing	94
265/3	Stock	.....	40	..	Healthy bones	112
263/3	Stock	.....	58	..	Healthy bones	110
272/2	3143	.....	32	..	Marked rickets	67
272/4	3143	.....	42	..	Marked rickets	59
273/1	3143	.....	49	..	Marked rickets	55
273/2	3143	.....	49	..	Marked rickets	52
273/5	3143	Healing factor	28	14	Advanced healing	80
273/6	3143	Healing factor	28	14	Advanced healing	77
272/7	Preventive	.....	32	..	Healthy bones	106
272/8	Preventive	.....	42	..	Healthy bones	110

globin might have had an antirachitic effect. In order to determine whether or not this was the case, hemoglobin was added to the rickets-producing diet or fed to animals which had been made rachitic by consuming diet No. 3143. Different samples of hemoglobin were used in these experiments. Merck's commercial hemoglobin, Pfanstiel's purified hemoglobin, crystalline oxyhemoglobin, made from ox blood by the freezing method of Offringa,[6] and also crystalline oxyhemoglobin obtained through the courtesy of Prof. L. J. Henderson, Harvard University, were used. All of these materials were analyzed and found to be practically free from phosphorus. The amounts of hemoglobin which were added to the diet varied from 1 to 15 per cent. In every case hemoglobin was substituted for an equivalent amount of gelatin, so that in

6. Offringa: Biochem. J. **28**, 1910.

rats fed with 15 per cent. of hemoglobin the diet contained no gelatin. The experiments were carried out in fifteen groups, with a total of seventy-six animals, and were both preventative, that is, the hemoglobin was given from the time when the rats were placed on a rickets-producing diet, and curative, that is, the administration of hemoglobin was commenced after rickets had already developed. The results of this series can be seen in Table 2, which contains some representatives of several groups.

TABLE 2.—*The Marked Antirachitic Effect of Hemoglobin*

(a) Prevention

No. of Lot and Rat	Diet	Hemoglobin Added	Days Mixture Fed	Necropsy Findings
268/1	3143	15% Merck	28	No rickets, perfectly normal bones
268/2	3143	15% Merck	42	No rickets, perfectly normal bones
268/3	3143	15% Merck	56	No rickets, perfectly normal bones
272/7	3143	15% Merck	32	No rickets, perfectly normal bones
272/8	3143	15% Merck	42	No rickets, perfectly normal bones
268/4	3143	Controls	28	Marked rickets
272/1	3143	Controls	56	Marked rickets
289/1	3143	10% Merck	28	No rickets, perfectly healthy bones
289/2	3143	10% Merck	42	No rickets, perfectly healthy bones
289/5	3143	5% crystalline	28	No rickets, perfectly healthy bones
289/6	3143	5% crystalline	42	No rickets, perfectly healthy bones
289/7	3143	2% crystalline	28	Marked rickets
289/8	3143	2% crystalline	42	Marked rickets
297/1	3143	Controls	28	Marked rickets
297/2	3143	Controls	42	Marked rickets

(b) Cure

No. of Lot and Rat	Diet	For Days	Hemoglobin Added	For Days	Line Test
273/5	3143	28	15% Merck	14	+++
273/6	3143	28	10% Merck	14	+++
281/1	3143	28	5% crystalline	9	+++
281/2	3143	28	5% crystalline	6	++
293/1	3143	28	2% crystalline	9	0
293/2	3143	28	2% crystalline	10	0
304/1	3143	21	5% crystalline	6	++
304/2	3143	21	5% crystalline	8	++
304/3	3143	38	None	..	0
304/4	3143	29	None	..	0

(c)

No. of Lot and Rat	Diet	For Days	Hemoglobin Added	For Days	Animals Kept	Line Test
274/5	3143	28	5%	8	In dark	+++
274/7	3143	28	5%	8	In dark	+++
274/1	3143	28	5%	8	In light	+++
274/6	3143	28	5%	8	In light	+++
274/3	3143	28	None	8	In light	0
274/8	3143	28	None	8	In light	0

The results in Table 2 show clearly that hemoglobin has a marked antirachitic effect when given in certain definite amounts. No rickets developed in rats which were put on diet No. 3143 containing 10 per cent. of hemoglobin when they were 40 or 50 gm. in weight. The growth curve of the animals was very little different from those kept on stock food (Curve 1). They were able to rear young on this diet. It will be seen that 5 per cent. is the smallest amount of hemoglobin which will

surely prevent the development of rickets. Given in smaller amounts the effect of the exhibition of hemoglobin will be uncertain, and rickets will develop on 1 or 2 per cent. of the substance just as if the rickets-producing diet had been fed unaltered. The same percentages of hemoglobin were needed to produce healing of rachitic animals. Certain differences were noticeable, however, in the type of healing in the bone from that caused by cod liver oil when different percentages of hemoglobin were given. Similar phenomena may be observed following the administration of other substances and will be considered later in more detail under the discussion of epinephrin and pilocarpin.

Since the hemoglobin molecule contains a chromophore and a globin group, it was of interest to know to which of the two the antirachitic action was due. Van Leersum [7] has recently stated that healing of rickets can be produced by the subcutaneous injection of solutions of hematoporphyrin. He believed that this healing might be due to the sensitization to light which is one of the well-known pharmacologic effects of this drug. In an endeavor to elucidate this question a 10 per cent.

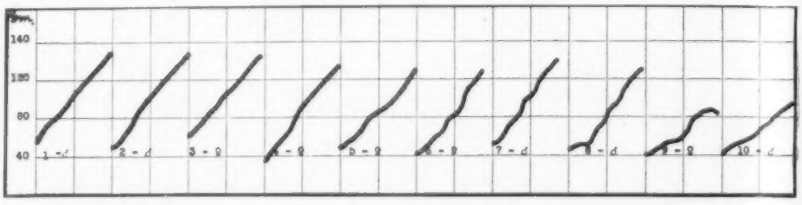

Fig. 1.—Numbers 1, 2, 3 and 4 received stock food; numbers 5, 6, 7 and 8 received Diet 3143, plus 15 per cent. of hemoglobin in place of 15 per cent. gelatin; numbers 9 and 10 received Diet 3143.

solution of oxyhemoglobin and 10 per cent. solution of hematin were injected subcutaneously into two groups of rats with rickets; rats with rickets were put in a light-tight compartment for eight days and fed on diet No. 3143 with 5 per cent. of hemoglobin. The 10 per cent. solution of hematin was derived from oxyhemoglobin after the method of Schulz.[8] It was somewhat alkaline. The method of preparation was roughly as follows:

Tenth normal hydrochloric acid was added to a salt-free solution of oxyhemoglobin. Alcohol was added to this mixture and the resulting liquid was extracted with ether. After evaporation of the ether, the residue was dissolved in a weakly alkaline solution.

The animals, which were kept in darkness, were placed in a large light-tight galvanized iron cage, the cover of which fitted closely, and having been supplied with food and water sufficient for eight

7. Van Leersum, E. C.: J. Biol. Chem. **58**:835 (Jan.) 1924.
8. Schulz: Arch. f. d. ges. Physiol. **38**.

days the cover was not removed until the end of that period. Special care was taken in all of these experiments to avoid any error which might result from partial starvation of the experimental animals. Not only were records of the growth of the animals kept, but also records of food consumption during the experimental period. It is to be emphasized that any injury to a rachitic animal, as, for example, indisposition and pain from hypodermic or intraperitoneal injection, may cause voluntary abstinence from food and healing as the result of starvation. The injections of oxyhemoglobin and hematin solutions caused no visible bad effect.

It is manifest from these experiments that hemoglobin given subcutaneously to the amount of 0.1 gm. is without antirachitic effect. The smallest amount of hemoglobin which can have a curative or preventative effect was found to be 0.5 gm. per day, given by mouth. The healing effect of hemoglobin cannot be due to a sensitization of the animal to light because the effect is obtained when animals in complete darkness are given hemoglobin; and finally, the antirachitic effect is apparently due to the globin fraction, since the chromophore group in the form of

TABLE 3.—*Results of Experiments on Rats*

No. of Lot and Rat	Diet	Days	After This Time Injections Given	Daily Food Consumption	Line Test
314/1	3143	21	3 × 1 c.c. of 10% hemoglobin.....	7–11 gm.	0
314/2	3143	22	3 × 2c.c. of 10% hemoglobin.....	7–11 gm.	0
312/2	2143	21	3 × 1 c.c. of 10% hematin.....	7–11 gm.	0
312/3	3143	21	3 × 2 c.c. of 10% hematin.....	7–11 gm.	0
329/2	3143	21	3 × 1 c.c. of full marrow extract...	7–11 gm.	++
329/4	3143	21	3 × 2 c.c. of full marrow extract...	7–11 gm.	+++
329/1	3143	21	3 × 1 c.c. extract without hemog...	7–11 gm.	++
329/3	3143	21	3 × 2 c.c. extract without hemog...	7–11 gm.	+++

hematin has no curative effect on rickets whatsoever. The amount of one injection of hematin, 1 c.c. of the solution, was equivalent to the exhibition of the amount of hematin in 2.5 gm. of hemoglobin.

Since the injection of 0.1 gm. of hemoglobin per day is not curative for rickets, the antirachitic effect of the marrow extract in which the total protein does not exceed 0.06 gm. per cubic centimeter must be due to another kind of protein. That this was the case was indicated also in a group of experiments in which the hemoglobin of the marrow extract was filtered off by means of a collodion ultrafilter of 3.5 per cent. acetic acid collodion. Injections of this hemoglobin-free extract to the amount of 1 and 2 c.c. were given every other day, for three times, to rats with rickets. A control group of animals was injected at the same time with the same amounts of unfiltered extract. In both groups the same results were obtained, namely, beginning healing after three doses of 1 c.c. each, and a little more advanced healing after three doses of 2 c.c. each. These results banished definitely the possibility that the antirachitic effect of the marrow extract might be due to its content of hemo-

globin, although they demonstrated that a sufficient amount of hemoglobin when mixed with the food can either prevent or heal rickets. Having obtained these results with animals, it seemed worth while to try whether hemoglobin was antirachitic also in man. With this end in view, two rachitic children on the service of Prof. John Howland in the Johns Hopkins Hospital were given hemoglobin. One of these children acquiring a bronchial pneumonia, the experiment in his case had to be discontinued shortly after its beginning. The history of the other was in brief as follows.

Fig. 2

Fig. 3

Fig. 2.—Roentgenogram showing the wrists of the patient, J. G., before treatment. Active rickets.

Fig. 3.—Healing of rickets after treatment with hemoglobin (patient J. G.).

REPORT OF CASE

History.—J. G., a boy, colored, aged 16 months, was admitted to Harriet Lane Home on March 23 with signs of marked rickets. On admission, the child was not able to stand or walk. The chostochondral junctions and the epiphyses of the long bones were enlarged. The inorganic phosphorus in the blood serum was 2.7 mg. per hundred cubic centimeters, and the roentgenogram showed severe rickets (Fig. 2). Without any other specific treatment, 5 per cent. of his daily food (cereal and milk) was replaced with an equivalent amount by weight of commercial hemoglobin. For a short time (two or three days) at the beginning of the experiment, the child showed an aversion to this food. He soon, however, began to relish it and consumed quantities according to his age. It may be remarked that before his discharge from the hospital he had acquired a liking for hemoglobin and refused food which was without this substance. Treatment with hemoglobin was begun on March 30. After forty-four days, a second analysis

of the blood serum showed the inorganic phosphorus to be 3.6 mg. per hundred cubic centimeters, the calcium 9.6 mg., and the calcium and phosphorus product 34.56. At the same time the child began to stand up in bed. After two weeks more, the inorganic serum phosphorus had reached the level of 4.2 mg. per hundred cubic centimeters, the serum calcium was 10.4 mg. and the calcium phosphorus product 43.68. Roentgenograms at this time (Fig. 3) showed marked healing with calcification of all epiphyses.

It seems logical from this experiment to hypothecate a possible relationship between the globin of hemoglobin and the specific antirachitic protein produced by the bone marrow. The structure of the globin is very similar to that of the histons, although there are certain differences, and, therefore, it was felt that it might be possible that this specific protein which was so powerfully antirachitic might be related to the histon group. Such an hypothesis seemed to be logical from another point of view. Guthrie and Brown claim to have found pressor and depressor substances in watery extracts of bone marrow, and these properties are, among others, those of the histons.

TABLE 4.—*Results of a Further Series of Experiments*

No. of Lot and Rat	Diet	Days	After This Time Added	Days	Line Test
320/1	3143	21	0.22% lysin	6	0
320/2	3143	21	0.22% lysin	9	0
320/4	3143	21	0.55% histidin	6	0
320/5	3143	21	0.55% histidin	9	0
321/1	3143	21	0.27% arginin	6	++
321/2	3143	21	0.27% arginin	9	++
321/3	3143	27	No addition	..	0
321/4	3143	50	No addition	..	0
322/3	3143	21	0.22% lysin, 0.55% histidin and 0.27% arginin	6	++
322/4	3143	21	0.22% lysin, 0.55% histidin and 0.27% arginin	9	++
322/5	3143	27	No addition	..	0
322/6	3143	50	No addition	..	0

Although only water-soluble proteins can be present in a watery extract, the chemical isolation of one water-soluble protein from a mixture presents difficulties and a shorter method was chosen to throw light on this question. Histons differ from other proteins chiefly in their content of the diamino-acids and the next group of experiments was planned to find out whether one or another of the diamino-acids might not have an antirachitic effect. Purified arginin, lysin and histidin respectively (Pfanstiel Company) were mixed with a rickets-producing diet in the same quantity that they are present in 5 gm. of globin. These mixtures were fed to different groups of rachitic animals. Another group of animals was given a diet containing a mixture of the three diamino-acids in the same proportions. Controls were kept for each group. The results of this series of experiments are contained in Table 4, which also shows that arginin has a specific antirachitic action, while histidin and lysin are inactive.

Monoamino-acids were studied also. These were cystin and tyrosin, and Table 5 shows the results of the administration of these substances to control groups of rachitic animals. Unfortunately, no other monoamino-acids were available in time to complete this series of experiments, but further studies of this group of substances are now in progress. It will be seen from this table that cystin is antirachitic when exhibited in large amounts.

Having progressed so far, I attempted to find out whether or not certain other biogenamins, to which group the diamino-acids belong, have any antirachitic effect. It seemed logical to try at first an amin which has physiologic actions similar to those of the histons, and the best known representative of this group of substances which fulfil these requirements was epinephrin. This substance was tested simultaneously with a drug having a similar pharmacologic effect, namely, pilocarpin. A word as to the technic of these experiments is necessary here. Albino rats are highly sensitive both to epinephrin and pilocarpin,

TABLE 5.—*Results of Administration of Cystin and Tyrosin to Rachitic Animals*

No. of Lot and Rat	Diet	Days	After This Time Added	Days	Line Test
317/1	3143	21	5% cystin	6	++
317/3	3143	21	5% cystin	9	++
327/2	3143	21	1% cystin	6	0
327/3	3143	21	1% cystin	9	0
307/1	3143	21	5% tyrosin	6	0
307/2	3143	21	5% tyrosin	9	0
317/4	3143	30		..	..
327/4	3143	30		..	..

whether these substances are injected subcutaneously or given per os. It was found necessary, therefore, to desensitize the experimental animals by giving them very small amounts of epinephrin and pilocarpin by mouth in their drinking water for a couple of days. In this way it was possible to increase the tolerance of rats to these drugs, so that after five or six days they were able to stand injections of 0.5 to 1 mg. of the drug, an amount which would have been fatal without preliminary oral desensitization with gradually increasing concentrations. The rachitic animals were given epinephrin or pilocarpin for from five to ten days. The epinephrin which was used in these experiments was of two sorts, the ordinary commercial epinephrin of Parke, Davis & Company and of Armour, which is sold in concentration of 1 : 1000 in physiologic sodium chlorid solution, and a crystalline l-epinephrin which was made by Prof. John J. Abel.[9] The results of these experiments are shown in Tables 6 and 7.

9. I wish to thank Dr. Abel for supplying me with this and with crystalline histamin, and for many suggestions about these materials.

TABLE 6.—*Effect of Pilocarpin on Rachitic Animals*

Rickety Rats Lot	Rat No.	Pilocarpin Administered	Days	Healing	Inorganic Phosphorus	Calcium	Ca : P Product
301	1	1:20,000 solution to water.....	2	Very marked	...	....	....
	2	1:15,000 solution to water.....	2				
	3	1:10,000 solution to water.....	2				
	4	0.5 mg. subcutaneously.....	2				
		1.0 mg. subcutaneously.....	2				
		Period of treatment.....	10				
306	1	1:20,000 solution to water.....	2	Beginning	...	....	....
	2	1:15,000 solution to water.....	2				
	3	1:10,000 solution to water.....	2				
		Period of treatment.....	6				
302	1	1:20,000 solution to water.....	2	Advanced	2.7	....	....
	2	1:15,000 solution to water.....	2				
	3	1:10,000 solution to water.....	2				
	4	1: 5,000 solution to water.....	2				
		Period of treatment.....	8				
315	1	1:10,000 solution to water.....	2	Very marked	3.3	10.0	36.3
	2	1: 5,000 solution to water.....	2				
	3	1: 2,500 solution to water.....	2				
	4	1: 2,000 solution to water.....	2				
		1: 1,500 solution to water.....	2				
		Period of treatment.....	10				
301	6	Controls without treatment.....		No healing	2.4	....	....
306	8						
325	6						

TABLE 7.—*Effect of Epinephrin on Rachitic Rats*

Rickety Rats Lot	Rat No.	Epinephrin Administered	Days	Healing	Inorganic Phosphorus	Calcium	Ca : P Product
276	1	1:20,000 solution to water.....	2	Beginning	...	....	....
	2	1:15,000 solution to water.....	2				
	3	1:10,000 solution to water.....	2				
		Period of treatment.....	6				
277	4	1:20,000 solution to water.....	2	Advanced	3.2	....	....
	5	1:15,000 solution to water.....	2		2.7		
	6	1:10,000 solution to water.....	2				
	7	1: 5,000 solution to water.....	2				
		Period of treatment.....	8				
283	1	1:10,000 solution to water.....	2	Very marked	2.2	....	....
	2	1: 5,000 solution to water.....	2				
	3	1: 2,500 solution to water.....	2				
	4	0.5 mg. subcutaneously.....	2				
		1.0 mg. subcutaneously.....	2				
		Period of treatment.....	10				
293	1	1:10,000 solution to water.....	2	Very marked	2.8	....	....
	2	1: 5,000 solution to water.....	2				
		1: 2,500 solution to water.....	2				
		1: 2,000 solution to water.....	2				
		1: 1,500 solution to water.....	2				
		Period of treatment.....	10				
328	1	1:10,000 solution to water.....	2	Very marked	2.0	10.0	19.2
	2	1: 5,000 solution to water.....	1				
		1: 2,500 solution to water.....	1				
		1: 1,500 solution to water.....	1				
		Period of treatment.....	5				
277	1	Controls without treatment.....		No healing	2.2	....	....
293	3				2.4		
328	3						
330	1						

The first signs of calcification in the metaphyses of animals treated with epinephrin and pilocarpin were visible after five days. After seven or eight days this calcification was much heavier, and the entire rachitic metaphysis was healed. If after a comparatively high concentration of the drug had been given, one or two subcutaneous injections were given in the last two or four days of the animal's life, the provisional zone of calcification was reformed also.

In the last group of rats treated with epinephrin the concentration of the drug was increased from 1 : 10,000 to 1 : 1,500 in five days. No subcutaneous injections of the drug were given to this group, but nevertheless the metaphysis was heavily calcified and the provisional zone of calcification was completely reformed. The blood serum of animals treated with pilocarpin and epinephrin and showing healing in the metaphysis was analyzed for inorganic phosphorus. It was found that the inorganic phosphorus varied from 2.2 to 3.4 mg. per hundred cubic centimeters. In several animals showing marked healing, the serum phosphorus was as low as that in the control animals which showed active rickets. In order to obtain all the data to control this extraordinary fact, in two groups determinations of the amount of calcium in the serum were also made. In one of these groups, the animals of which were treated for eight and ten days with pilocarpin, the product of serum calcium × serum phosphorus reached 36, but in another group treated only for six days with rapidly increasing concentrations of epinephrin, in which the animals showed very advanced healing with reformation of the provisional zone of calcification and calcification of the metaphysis, the calcium-phosphorus product remained lower than 20, as low a level as is usually seen with acute rickets. The food consumption and growth of animals treated with epinephrin and pilocarpin was especially carefully controlled, to avoid any possible complications due to starvation. It was found that pilocarpin when begun in a relatively high concentration could cause loss of appetite, but if an initial concentration of 1 : 20,000 was given from one to two days in the drinking water, no toxic effects were seen. The administration of epinephrin can be started at a concentration of 1 : 10,000 without loss of appetite and with good growth, but sudden death may result from administration of this drug in this concentration in a certain number of animals.

A group of animals at the same time was treated with histamin, and the same technic was used in giving this drug as was used for the exhibition of epinephrin and pilocarpin, that is, the substance was dissolved in the animals' drinking water when administered per os. The histamin was given in a concentration varying from 1 : 10,000 to 1 : 2,500.

Some other groups of animals were studied for the effect of acidification or alkalinization on rickets. In the acidification experiments one

group of animals was given 5 gm. of hydrochloric acid in 95 gm. of Diet 3143. This acid was poured on the wheat gluten of the diet, the resulting paste was allowed to dry, reground and mixed with the food. Another group was given 0.2 per cent. hydrochloric acid in their drinking water. Still another group was given 5 per cent. of sodium carbonate and another 5 per cent. of sodium bicarbonate in the rickets-producing diet. All these groups gave perfectly negative results, as is shown in Table 8.

COMMENT

The experiments here described form a series, as they demonstrate that proteins play a rôle in bone formation since they show the anti-rachitic properties of certain protein substances and their kindred amins. Moreover, because of these results, the series is directly connected with former experiments which have been reported elsewhere, and which are extended by these. In the former experiments, emphasis was placed

TABLE 8.—*Groups of Rats Giving Negative Results*

No. of Lot and Rat	Diet	Days	After This Time Added	Days	Line Test
309/1	3143	21	Histamin in 0.02, 0.04 and 0.05% to water	6	Negative
309/2	3143	21		9	Negative
309/3	3143	21		11	Negative
310/1	3143	21	5% Na_2CO_3 to food	6	Negative
310/2	3143	21	5% Na_2CO_3 to food	9	Negative
311/1	3143	21	5% $NaHCO_3$ to food	6	Negative
311/2	3143	21	5% $NaHCO_3$ to food	9	Negative
319/1	3143	21	5% HCl to food	9	Negative
319/2	3143	"	5% HCl to food	11	Negative
328/1	3143		2% HCl to water	9	Negative
328/2	3143	7½	0.2% HCl to water	14	Negative
309/4	3143	27	"	..	Negative
310/4	3143	30	"	..	Negative
328/3	3143	33	"	..	Negative

on the influence exerted by a protein substance in the process of osteogenesis. The nature of this protein can be logically inferred from the results of the experiments recorded in this paper. Other studies are going on, the results of which it is expected and hoped will permit the definite determination of this protein and its isolation from the marrow. But since the recovery of such a substance is a tedious and difficult process, it seemed legitimate to carry on the experiments reported here with purified substances which were available ready prepared, so that the work done with the isolated protein might be confirmed and strengthened by the inferences which it is possible to draw from the results here described. From previously published data and from the data recorded here, a succession of premises seems justified. In the first place, it was shown that proteins exist with a specific influence on ossification. In the second, such a protein was shown to be a product of the bone marrow and to be water soluble. This protein, moreover, was not an albumin nor could it have been one of the globulins, since the latter are pratically

insoluble in water. The work of Brown and Guthrie [10] gave evidence that among the water-soluble proteins of the marrow, pressor and depressor substances exist. These properties are characteristics of histons, and in the experiments reported in the foregoing an antirachitic action was found to be associated with the globin fraction of hemoglobin which is one of this group of substances. At the same time, however, it was shown that the antirachitic power of globin is far inferior to that of the specific protein produced by the marrow. In order to produce healing it was necessary that the animals should consume 0.5 gm. of hemoglobin a day for from six to ten days, 0.5 gm. of hemoglobin being equal to 0.47 gm. of globin, whereas healing is produced in the course of a week by the administration of 0.18 gm. of the marrow protein. Twice this amount of hemoglobin has no antirachitic action even though given subcutaneously. The explanation of these differences is afforded by the results of the experiments in which rachitic animals are treated with diamino-acids. The amount of arginin which is contained in 5 gm. of globin (0.27 gm.) was sufficient to induce a beginning healing of rickets in six days. The globin of hemoglobin differs chiefly from other histons in its content of arginin, which is much lower than the amount of arginin in other members of this group. Other histons may contain five times as much arginin as is found in globin, and experiments which are now under way it is hoped will answer the question as to whether or not the antirachitic potency of the before-mentioned marrow protein is due to a high content of arginin. Moreover, experiments are also under way concerning the antirachitic effect of protamins and other protein substances with a high arginin content.

It is possible that the failure of extracts composed of rachitic bone marrow to act as an antirachitic substance may be explained in view of the findings recounted here. Other organs than the bone marrow under normal conditions produce histons, for example, the liver, and it is well known that under pathologic conditions the histons may disappear from organs which normally produce them. This is true in acute yellow atrophy of the liver.

On the other hand, the presence of histons in other organs of the body may explain the antirachitic effect obtained from the administration of organ extracts, for example, those of the endocrine glands (Langstein and Vollmer). If this is the case it is not necessary to hypothecate antirachitic hormones, but it is simply necessary to assume the supply to the body by endocrine therapy of a missing product, histon, which is present under normal conditions.

On the basis of histon healing it is possible to offer an hypothesis of the mechanism of the healing of rickets in experimental animals as

10. Brown and Guthrie: Am. J. Physiol. **14**:328; ibid, **18**:110.

the result of starvation. Because of the tissue disintegration which is consequent on starvation, decomposition of protein molecules takes place, and as a result the amino-acid liberated will be transported all through the body in the blood stream. One of the results of such an auto-injection of amino-acid may be the precipitation of tertiary calcium phosphate in rachitic tissues, in which no such process could have taken place otherwise. Moreover, it is not too presumptuous to suspect that the well-known growth-promoting property of protein substances may be partly in relation to their efficiency in promoting osteogenesis, which is an important and specific part of growth. MacDougall's [11] and Ackroyd and Hopkins' [12] experiments would seem to indicate that the growth-promoting property of different proteins is dependent on their content of amino-acids. It is not possible at the present time to explain the antirachitic effect of cystin. It should be emphasized in this connection, however, that a large amount of this substance is necessary in order that it may show an antirachitic effect. Arginin is active in amounts as small as 0.27 gm., but cystin has to be given in as high a concentration as 5 per cent. of the diet in order that it may cure rickets. It is necessary to believe at the present time that the antirachitic action of amino-acids is specific for each acid which reacts in this way, and it is not characteristic of a group as a whole, for example, tyrosin even in amounts as great as 5 per cent. of the total food intake is absolutely without healing influence on rickets. Cystin, besides, differs from other mono-amino acids in the fact that it is a double amino-acid and hence is more closely related to arginin than any other member of the same group. Moreover, Howland, Kramer and Shipley [13] have shown that certain proteins and combinations of amino-acids, for example, egg albumin, do not favor but rather delay the process of calcification, and moreover, the serum proteins exert no antirachitic effect (personal communication). It is not possible in this place to discuss any influence which the basic character of the protein (the electro positive charge) may have to do with their antirachitic potency. Nearly all the biogen amins are bases, but their physiologic effects could hardly be explained solely on the basis of this property. Furthermore, alkalinization and acidification of the rickets-producing diet have no visible effect on the course of the disease. The alkalinization was very extreme. Bethe and Rohde [14] claim to have produced an extreme alkalinity of both blood and tissues by diets such as the one which I used. In passing, the results which were obtained from feeding highly acidified food definitely

11. MacDougall: Proc. Soc. Exper. Biol. Med. **19**, 1921-1922.
12. Ackroyd and Hopkins: Biochem. J. **10**, 1916.
13. Howland, Kramer and Shipley: Proc. Am. Pediat. Soc., 1925.
14. Bethe and Rohde: Arch. f. d. ges. Physiol. **182**:114, 1920.

contradict the belief which has been stated by some authors in the curative action of acidification.

Concerning the experiments with epinephrin and pilocarpin, Stöltzner first recommended the administration of epinephrin to rachitic children as a form of endocrine therapy, but the experiments which are here recorded were made from a different point of view. Epinephrin is related to the histon group physiologically, since among the biogen amins it has the most marked pressor and depressor action. And, moreover, epinephrin is generally supposed to be derived from an amino-acid, although no sufficient proof of this idea has yet been brought forward (Guggenheim).[15] Pilocarpin is an alkaloid which it seemed worth while to study because of its similarity in physiologic action to epinephrin, and it has been suggested that the alkaloids may be related to the biogen amins and so indirectly to the proteins. After preliminary trials, it was found that by commencing with very dilute solutions and by gradually increasing their strength until the animals were taking a high concentration of epinephrin and pilocarpin, their toxic effects could be avoided and a certain amount of desensitization accomplished, in agreement with the findings of Cushny [16] and Abderhalden.[17] By these means a beginning healing could be produced in from five to eight days by dilute solutions (1:20,000 and 1:10,000). It is necessary here to discuss somewhat in detail the difference in the type of healing of rickets induced by these drugs and by cod liver oil. Cod liver oil in therapeutic doses at first causes the recalcification of the epiphyseal-diaphyseal border of the cartilage, and calcification of the osteoid tissue in the rickety metaphysis occurs only later. Under the influence of low concentrations of epinephrin and pilocarpin, the precipitation of calcium phosphate goes on first in the metaphysis. This form of healing continues until about the tenth day of the administration of the drug, when the whole metaphysis is usually found calcified up to the cartilage. If higher concentrations are used at the beginning of the course of treatment, for example, 1:10,000, increasing in six days to a concentration of 1:1,500, the healing of the rickets will be accelerated, and, simultaneously with calcification of the metaphysis, the provisional zone of calcification of the cartilage will be reformed. These different types of healing are shown in Figures 4, 5 and 6. Similar phenomena are observed when rachitic animals are treated with hemoglobin. When healing is brought about by the exhibition of 5 gm. of hemoglobin, calcification occurs first in the metaphysis and is quite regularly laid down, differing thereby from the scattered calcification found in the bones of rats which are beginning.

15. Guggenheim: Die biogenen Amine, Berlin, 1920.
16. Cushny: Pharmacol. J. **46**, 1908.
17. Abderhalden and Kautsch, quoted by Guggenheim.

to heal spontaneously. When larger amounts, that is, 15 gm. of hemoglobin are given, the reformation of the provisional zone of calcification and heavy calcification of the metaphysis occur simultaneously.

When slight calcification of the metaphysis was first observed in the early experiments with epinephrin, it was deemed worth while to establish with certainty the fact that slight calcification in the rachitic metaphysis could be interpreted as true healing, and, therefore, the inorganic phosphorus in the blood serum of these rats which are treated with epinephrin was determined. The determinations demonstrated the rather surprising fact that there was no difference between the serum phosphorus of the healing animal and that of the untreated controls at the beginning of the healing. After the tenth day of the treatment the inorganic phosphorus of the serum began to increase, however, and the

Fig. 4

Fig. 5

Fig. 4.—Bone from a control rat with active acute rickets. Cross free-hand section stained with silver nitrate, × 6.

Fig. 5.—Bone prepared as described in Figure 4. This bone was taken from an animal with healing rickets which was treated with hemoglobin given in the amount of 5 per cent. of the diet. The calcification of the metaphysis is advanced, but there is no attempt at reformation of the provisional zone of calcification.

calcium × phosphorus product rose above 30. These determinations were done repeatedly, and in one of the most characteristic groups of animals treated with epinephrin, animals which showed marked healing with both reformation of the provisional zone of calcification and calcification of the metaphysis, the blood had an inorganic phosphorus content of 2 mg. per hundred cubic centimeters and a calcium content of 9.6 mg., giving a product of 19.2. This product would indicate acute rickets in the animals from which the blood serum was drawn. Nevertheless, marked healing was unmistakably demonstrated by histologic

examination of all the bones of the animals. These animals had been treated with epinephrin for five days. The drug was administered at the beginning of the treatment in a concentration of 1 : 10,000, and the strength of the solution was increased gradually until the concentration of the drug was 1 in 1,500. With a daily water intake of from 5 to 8 gm. (the drug was given in drinking water) the total amount of epinephrin consumed by each animal amounted to from 7.3 to 11.6 mg. in five days. This result, which is to be regarded as the most important of all the findings recorded in this paper, shows that healing of rickets with the deposition of calcium in the bones can take place with a low product of calcium × phosphorus in the serum. The agent which caused this healing is quite unimportant. The histologic findings, in conjunction with the chemistry of the inorganic calcium and phosphorus in the

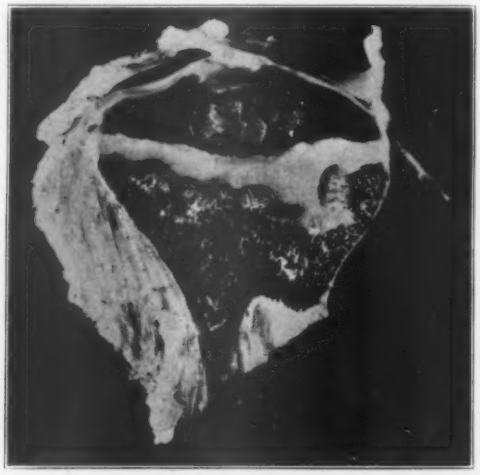

Fig. 6.—Bone from an animal treated with epinephrin for 10 days. Concentration of the drug was increased in this time from 1 : 20,000 to 1 : 5,000. Calcification of the metaphysis is complete but there is no calcification of the cartilage.

serum, are the really significant facts which resulted from this experiment. It is certain that calcification can take place in the body of an animal whose blood serum contains calcium and phosphorus which give a product of below 20. This cannot otherwise be explained than by the assumption that recalcification of rachitic bone is a primary condition which takes place as a consequence of a local change within the tissue itself. The augmentation of the inorganic phosphorus of the serum is a secondary sequella of the local calcification.[18]

18. Some of these determinations, especially the one which has been described in detail, were kindly confirmed by Dr. Benjamin Kramer, who did the analyses of the serum for calcium and phosphorus.

As to the mechanism of the healing of rickets produced by epinephrin and pilocarpin, there are many possible explanations. It may be that either can imitate or replace certain amino-acids, and in this way act therapeutically by way of substitution. On the other hand, it is known that epinephrin among its manifold pharmacologic actions is an efficient stimulant to the function of hematopoesis (Edmunds and Nelson),[19] and it is imaginable that a parallel stimulation of the other functions of the marrow may be induced coincidently by this drug.

The comparison of the chemical structure of the antirachitic substances yields nothing of any definite significance at the present time. Histidin, histamin and pilocarpin all contain the imidazol ring, but only

Fig. 7.—Bone of an animal treated with epinephrin for five days. Concentration of the drug was increased in this time from 1:10,000 to 1:1,500. This bone shows primary reformation of the zone of provisional calcification and some recalcification of the metaphysis.

pilocarpin is antirachitic. The structure of epinephrin is related to that of tyrosin but epinephrin causes the healing of rickets and tyrosin does not. Cystin and tyrosin are both derivatives of alanin, but tyrosin is devoid of the antirachitic action which cystin shows. These differences are not astonishing if we consider that very small alterations of the chemical structure change the steric composition of the atom. A change from the ϵ-amino position to the α-amino position is able to induce very considerable differences in the physiologic property of a substance.

19. Edmunds, C. W., and Nelson, E. E.: J. Exper. Med. **41**:1 (Jan.) 1925.

CONCLUSIONS

1. Certain proteins, presumably histons, with a high content of arginin, play an important rôle in the process of normal ossification. These substances are produced in the bone marrow.

2. Certain amins and physiologically similar alkaloids induce the healing of rickets presumably by stimulating the bone marrow.

3. Hemoglobin induces the healing of rickets not only in rats but also in children.

4. The primary event in the healing of the rickety process in the bone is its calcification due to local alterations in the rickety tissue. The changes in the chemical constitution of the blood serum, especially as regards the inorganic phosphorus, though they follow calcification of the bone very rapidly, are of a secondary nature and are sequellae of the calcification.

INTRATHORACIC TUMORS IN CHILDREN

REPORT OF A CASE *

HUGH L. DWYER, M.D.
AND
FERDINAND C. HELWIG, M.D.
KANSAS CITY, KAN.

Tumors within the chest cavity are extremely rare in childhood. Most of those reported occupy the mediastinal space, arising from the structures contained therein, or are embryonal in character.

The occurrence of a sarcoma in a child, arising from the inner aspect of a rib and filling the right thoracic cavity, is of such rarity that we believe the following case report is of interest.

REPORT OF CASE

History.—A boy, aged 12 years, came to the outpatient department in 1919, complaining of being easily tired, of losing weight and of elevations of temperature in the evenings. His father died of pulmonary tuberculosis in 1917. A positive Pirquet and a 4 plus Wassermann reaction were the only positive findings at that time. Antisyphilitic treatment was followed indifferently until 1923. The boy occasionally complained of cough, loss of weight and abdominal pain. Nov. 26, 1924, he was admitted to the hospital, with cough, pain in the right side of the chest and back. He stated that his voice had been getting "husky" for several weeks.

Physical Examination.—The patient was a poorly nourished, well developed boy, weighing 89 pounds. There was dyspnea on exertion and slight orthopnea. There was a painless swelling on the right side of the chest, at the third interspace in the midclavicular line, which had a broad base, 6 cm., and protruded from the chest wall about 3 cm. It was not painful on palpation. It apparently was noninflammatory, and of the consistency of rubber. It could be completely reduced within the thorax, causing but little pain. The intercostal spaces were obliterated over this side, and there was little respiratory excursion. The superficial veins were prominent over the entire thorax, but more so on the right. A slight enlargement of the right axillary and epitrochlear glands was found.

The breath sounds were absent from the right apex to the fifth rib, and this area was dull or flat on percussion. Below the fifth rib, the breath sounds were distant, a few mucous râles were present, and at the base there was evidence of fluid. Posteriorly, the breath sounds came through well.

On the left side, with the exception of enlargement of the heart to the left—the maximum impulse being in the sixth interspace—the findings were apparently normal.

The symptoms were those of an effusion, but the location and the history were unusual and a tentative diagnosis of intrathoracic tumor was made.

A roentgenogram taken on November 26 showed, "A large circumscribed opacity, homogeneous and dense, involving the central portion of the right lung field. The right diaphragm is high, flattened and fixed. The apex is clear. The findings suggest encapsulated fluid with pleurisy at the base."

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* Received for publication, July 11, 1925.

* From the Department of Pathology, University of Kansas and the Children's Mercy Hospital.

During the next few weeks, the temperature fluctuated between 100 and 102 F., and the voice became quite husky. Weakness, labored breathing and dilation of the veins of the trunk were the main symptoms. The heart became displaced to the left to such an extent that the area of cardiac dulness extended to the axillary line. The breath sounds on the right could be heard only over a small area posteriorly below the spine of the scapula; over the left side of the chest the normal vesicular breathing was replaced by bronchial breath sounds with numerous sibilant and moist râles.

The chest was aspirated on several occasions, always from the lower thorax, from 750 to 1,900 c.c. of bloody fluid being removed without appreciable change in the physical or roentgenographic findings. Only punctures below the eighth rib were successful.

On one occasion after 1,900 c.c. was removed, the radiologist reported, "Complete dense opacity of the entire right lung field with wide displacement of the heart and mediastinal shadows."

Laboratory Findings.—The sputum was negative for tubercle bacilli. The blood showed erythrocytes, 3,300,000; leukocytes, 8,500; hemoglobin, 70 per cent. (Dare); neutrophils, 78, and lymphocytes, 22. Urinalysis showed a moderate amount of albumin and few granular casts. Aspirated fluid had a specific gravity of 1,026; the first part coagulated, the larger part did not. It contained many red blood cells and no organisms were found.

The youth died Jan. 3, 1925, one month after admission.

Necropsy.—The body was that of a well-developed and poorly nourished boy. The right side of the thorax was larger than the left, and at the third interspace in the midclavicular line was a soft mass measuring 6 by 3 cm. A small amount of bloody fluid aspirated from this mass did not change the size and character noticeably.

The abdominal cavity was found normal with all the organs in normal position except the liver, which extended 10 cm. below the costal border. The organs were essentially negative except the kidneys which were enlarged, each weighing 120 gm., and showing some mottling on the surface.

A dark grayish bloody mass filled the right thoracic cavity extending across the median line, displacing the heart and left lung to the extreme left. The right lung was found flattened against the posterior thoracic wall and dorsal vertebrae. It was about the size and shape of the boy's hand.

The lower part of the right thoracic cavity contained a space filled with about 2,500 c.c. of bloodtinged fluid. The floor of this cavity was formed by the diaphragm and the roof by the base of the tumor. The fluid extended up around the tumor to the line at which it adhered to the thoracic wall, at about the eighth rib.

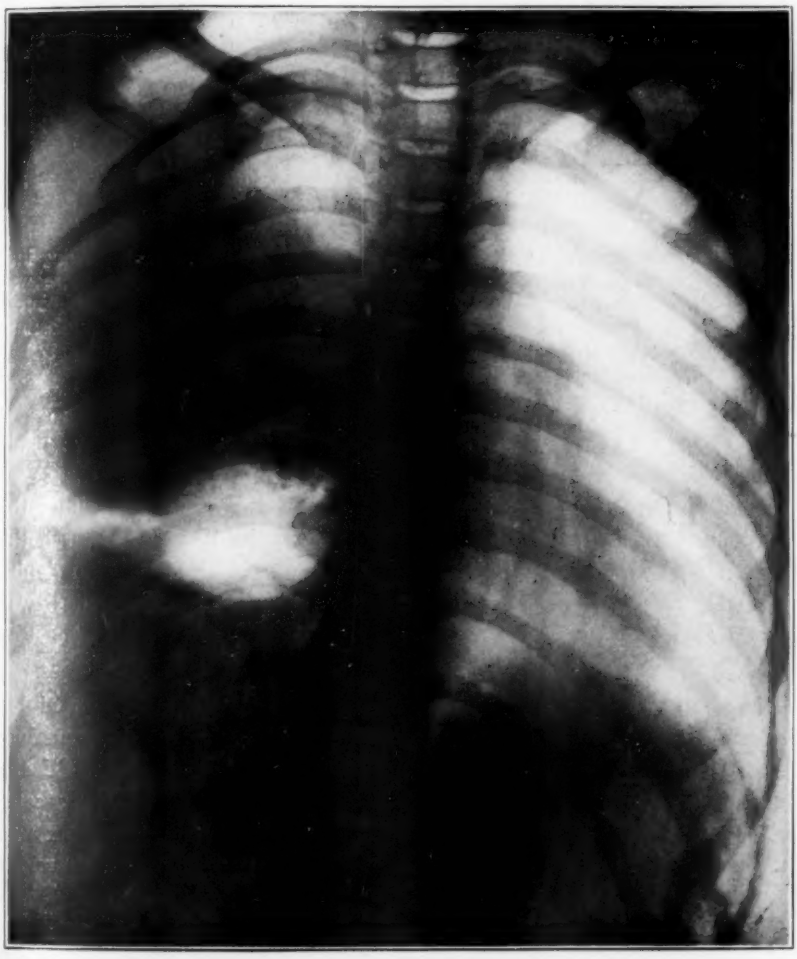
The tumor stripped easily from the thoracic wall to which it adhered at every place of contact, except on the inner aspect of the third to the sixth rib, anteriorly, when the attachment was so firm that portions of the rib were left with the tumor for further examination. The growth was adherent to the mediastinal structures but not to the lungs. The thymus was not involved.

Examination of the tumor mass after removal showed it to be growing from the region of the fifth rib about 2 to 3 cm. posterior to the costochondral articulation. It was semicystic, had no capsule and had undergone marked degeneration with hemorrhage, to such an extent that the major portion, particularly as it approached the mediastinum and grew away from its source at the ribs, was little more than a mass of clotted blood, containing scattered pale, cellular grayish-pink friable tissue. There was no gross evidence of infiltration of the lung and apparently the mediastinal and hilum nodes were not invaded although many of them were hyperplastic.

The right lung was extremely atelectatic from compression and the pleura was shaggy. From the surface, clotted blood and shreds of tumor tissue could easily be separated. On section, the atelectatic lung showed some healed calcified

nodules, and in the apex of the left lung similar healed nodules were found. Three calcified tuberculous nodules were found among the hyperplastic nodes at the hilum.

Search for the origin of the tumor showed it to be growing from the fifth rib, not involving the neighboring ribs except to displace them by pressure. The parietal pleura for a distance of 5 or 6 cm. from the site of origin was missing. The affected rib was replaced in its proximal two-thirds by the tumor.



Roentgenogram showing tumor in the right thoracic cavity.

A number of sections taken from the mass in different areas presented a variety of pictures. A block from near the lung hilum presented a mixed cell tumor with marked variation in the size, shape and staining of the cells. Large pink-staining tumor giant cells were encountered, intermingled with masses of round and spindle cells. All types of mitotic figures were seen. There was considerable edema and the stroma varied in amount in different fields. The cells lay on unlined blood spaces in many areas, and everywhere there was a tendency toward degeneration and hemorrhage.

Another section taken from an area as far distant from the apparent source as possible showed several spicules of bone and numerous islands of undifferentiated cartilage cells. The bone showed irregular calcification, large lacunae and no Haversian canals.

Sections through the suspected rib showed numerous cystic and incompletely formed areas of bone and cartilage. Here the bone appeared even less fully differentiated and areas of direct transition from atypical cartilage into these bony spicules could be seen. The spicules were surrounded by small islands of pale staining embryonic cartilage cells, and irregular tumor cells.

Direct invasion of the intercostal muscles by the spicules of bone and cartilage was noticed, and here as elsewhere there was a tendency to hemorrhage and degeneration.

The lung sections showed compression atelectasis and a chronic diffuse interstitial fibrosis with healed and calcified tubercles.

The hilum and mediastinal nodes showed healed tuberculosis and those not thus involved presented the picture of acute lymphadenitis.

The kidneys showed acute tubular nephritis.

Pathologic Diagnosis.—An osteochondra-sarcoma of the fifth rib, growing into the thoracic cavity, showing marked hemorrhage and degeneration. There was compression atelectasis of both lungs, very pronounced in the right, with interstitial fibrosis. Calcified and healed tuberculosis of the lungs and mediastinal glands was apparent. There was acute tubular nephritis.

REVIEW OF THE LITERATURE

The early recognition of this condition would probably have made it easily amenable to surgical treatment. It is remarkable that even after attaining an enormous size, the tumor did not incapacitate the youth until the last month of his life. From the time he entered the hospital until death, the mass increased rapidly in size, due, no doubt, principally to the amount of hemorrhage. In fact, when the chest was opened at necropsy, the appearance was that of a large mass of clotted blood.

In the cases collected by Hedbloom,[1] and in a large series of his personal cases, is seen a marked tendency to recurrence after operation, not only of sarcoma but also of chondroma and fibroma. Of the 213 collected cases of tumors of the bony chest wall, 78.7 per cent. were tumors of the ribs, and the anterior aspect of the right thorax was the most common site. Only three of this series were in patients under 10 years of age.

A case similar to our own is reported by Heuer,[2] in which he removed a recurrent osteochondrosarcoma of the tenth rib in a girl, aged 14 years. Wiesmuller[3] also reported a chondroma of the chest wall growing into the mediastinum.

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1. Hedbloom, C. A.: Tumors of the Bony Chest Wall, Arch. Surg. **3**:56 (July) 1921.

2. Heuer, George J.: Ann. Surg. **79**:687, 1924.

3. Wiesmuller: Quoted by Graham, Footnote 6.

Roberts,[4] in his discussion of the origin of intrathoracic tumors, designates the sites of origin as follows: "(*a*) either lung, which is not very common; (*b*) pleura or subpleural tissue; (*c*) thoracic wall—this applies particularly to osteosarcoma or osteochondrosarcoma, growing in from the bony framework of the chest; (*d*) mediastinal structures, particularly the lymphatic glands, and the fat and cellular tissue; (*e*) the bronchi, trachea, oesophagus . . .; (*f*) pericardium, and (*g*) thymus."

Kroenlein[5] reported a lipoma growing inward from the chest wall of an infant.

Primary new growths of the lungs, pleura and pericardium are practically unknown in children. Carcinoma from the epithelial structures of the posterior mediastinum, fairly frequent in adults, are, according to Graham,[6] so rare in childhood that a report of such raises a doubt as to the correctness of the diagnosis.

Most of the primary tumors of the mediastinum are dermoid cysts, teratomas and lymphosarcomas. Ewing believes that most of the lymphosarcomas arise from the thymus and considers them varieties of thymoma.

Smith and Stone have recently collected the reported cases of dermoids and solid teratomas, and found that twelve of the 125 cases occurred in children.

SUMMARY

A case of intrathoracic osteochondrosarcoma in a youth is reported. The tumor originated from the inner aspect of the fifth rib, almost filled the right thoracic cavity, producing atelectasis of the right lung and displacement of the heart and mediastinal structures.

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4. Roberts, F. T.: Albutt System of Medicine, Vol. 5, New York, The MacMillan Company, 1909.
5. Kroenlein: Quoted by Graham, Footnote 6.
6. Graham, E. E.: Abt's Pediatrics, Vol. 4, Philadelphia, W. B. Saunders Company, 1923.

BASOPHILIC AGGREGATION IN THE NEW-BORN*

ALFRED FRIEDLANDER, M.D.
AND
CHARLOTTE WIEDEMER, M.D.
CINCINNATI

It has been known for a long time that a basic staining substance is present in certain erythrocytes. By appropriate staining methods, this can be demonstrated as basophilic stippling, polychromatophilia or reticulation of these cells.

Polychromatophilia appears as a diffuse double staining of the red cells; stippling shows as small deep blue granules. The reticulation—demonstrated best by supravital stains, such as brilliant cresyl blue—appears as a delicate network in various forms.

It is probable in the light of modern researches that polychromatophilia, basophilic stippling and reticulation are merely different manifestations of the same process. This deduction, first made by Hawes,[1] was confirmed by Schilling-Torgau.[2]

It is now quite generally believed that these basophilic forms are young (or immature) erythrocytes. The grounds for this belief are thus summarized by Key.[3]

In the circulating blood of normal adult humans, no polychromatophilia or punctate basophilia and not over 1 per cent. of reticulated cells are found.

In the blood of mammalian embryos the basophilic erythrocytes occur frequently and their percentage decreases as the age of the embryo advances.

Shortly after birth the erythrocytes of the circulating blood resemble those of the adult.

Basophilic substance can usually be demonstrated in nucleated red blood cells.

In adult bone marrow, where blood formation is in progress, basophilic erythrocytes are common.

In anemic adults the percentage of basophilic erythrocytes is roughly proportional to the activity of the bone marrow.

The theory that basophilic erythrocytes are old senile erythrocytes is no longer tenable.

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* Received for publication, June 3, 1925.
* Read before the American Pediatric Society, Washington, D. C., May, 1925.
* From the Department of Medicine, College of Medicine, University of Cincinnati.

1. Hawes: A Study of Reticulated Red Cells by Means of Vital Staining, Boston M. & S. J. **161**:493, 1909.

2. Schilling-Torgau: Folia haemat. **11**:572, 1911; **14**:97, 1913.

3. Key, J. A.: Studies on Erythrocytes, Arch. Int. Med. **28**:511 (Nov.) 1921.

It is now generally believed that the study of the basophilic cells affords an approximate indicator of the presence of young cells in the circulating blood—in that these cells are evidences of the extrusion of immature cells into the circulation. It is also possible that the percentual incidence of the basophils may be of clinical value in the study of blood regeneration in certain forms of anemia. As Key [3] has said: "Since the form of the reticulation varies in pathologic anemias and in anemias due to hemorrhage, it is felt that a careful study of the morphology of the reticulation in the various types of anemia may be of some value clinically."

As a preliminary to the study of the basophils in pernicious anemia—now under way—we felt that a survey of the blood of the new-born, with reference to basophilic aggregation, would be of interest. The

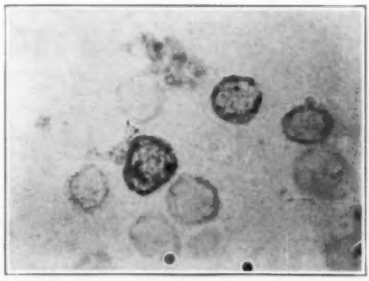

Fig. 1.—Infant, 12 hours old; methylene blue stain; × 1,000.

studies here reported have to do with basophilic aggregation in the new-born. The work on lead colic and certain of the anemias is reserved for future publication.

TECHNIC

The demonstration of basophilic aggregation is a very simple process. We have used three methods.

1. Stained smears. We used three different stains. We began with the stain advocated by McCord [4] and his associates in their work on the diagnosis of lead poisoning. This is a 2 per cent. solution of methylene blue, diluted with distilled water until the fluid is just translucent to light. Later, we changed to Goodpasture's polychrome methylene blue, which was found to show the granules more distinctly (Figs. 1, 2 and 3).

A 5 per cent. aqueous solution of brilliant cresyl blue was also tried, but was not found to be as satisfactory as the polychrome methylene blue.

4. McCord, C. P.; Minster, D. K., and Rehm, M.: Basophilic Aggregation Test in Lead Poisoning, J. A. M. A. **82**:1759 (May 31) 1924.

A thick smear of blood is made on a glass slide. Without fixing, this is stained for ten minutes with one of the before-mentioned stains. (It is necessary to have thick smears. Smears as ordinarily made for blood staining will not do.) After staining, the smear is gently washed in tap water and air dried.

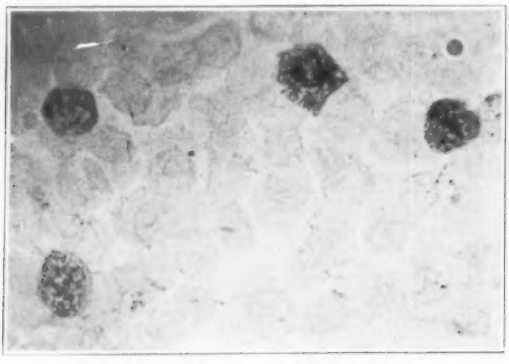

Fig. 2.—Infant, 12 hours old; polychrome methylene blue stain; × 1,000.

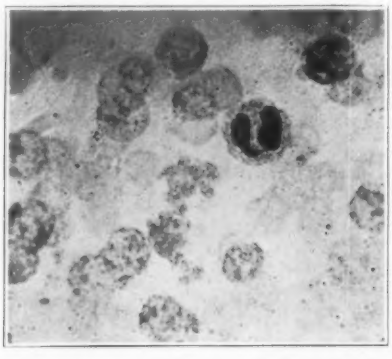

Fig. 3.—Infant, 1 hour old; polychrome methylene blue stain; × 1,000.

The erythocytes are hemolyzed and usually somewhat swollen. The normal reds, indeed, show as mere faint shadows while the basophilic cells show blue granules of varying size, distributed throughout the cells.

A rough quantitative estimate of the number of basophilic cells is had (according to the method of McCord).[4] The average of the number of such cells found in ten oil immersion fields is taken. A result is called negative when there is only one basophilic cell to two or three fields, A + 1 means that there is one basophilic cell to the field, + 2, two basophilic cells, and so on (Table 1).

TABLE 1.—*Approximate Quantitative Estimation of Basophilic Aggregation in the New-Born. (Stained Smear.) Tests Made at Twenty-Four Hour Intervals*

Sex *	Color	Age	Days 1	2	3	4	5	6	7	8	9	10	11
♂	W	12 hours.....	10	10	8	6	6	5	4	2	2	1	Neg.
♂	C	12 hours.....	10	10	9	8	8	6	5	3	3	1	Neg.
♂	W	12 hours.....	10	9	8	7	7	5	3	1	Neg.	..	.....
♂	W	12 hours.....	10	10	9	7	6	4	3	3	1	Neg.	.....
♀	W	1 hour.....	10	10	9	6	?	1	1	1	Neg.	..	.....
♂	C	4 hours.....	10	10	8	6	4	2	2	1	Neg.	..	.....
♀	W	12 hours.....	10	10	10	6	3	3	3	1	Neg.	..	.....
♂	W	12 hours.....	10	10	8	6	5	4	4	3	2	Neg.	.....
♀	C	10 hours.....	10	10	9	8	8	6	5	3	2	Neg.	.....
♀	C	5 days.....	..	..	..	..	5	3	2	1	1	Neg.	.....

* In this column, ♀ indicates female; ♂ male.

2. In order to obtain more accurate quantitative estimates of the number of basophilic cells in the blood of the new-born, the following procedure was adopted.

We used a blood pipet and counting chamber. The combined stain and diluent was made up as follows:

5 per cent. aqueous solution brilliant cresyl blue.....	1 c.c.
Distilled water	2 c.c.
Physiologic sodium chlorid solution.....	2 c.c.

The pipet for doing a white cell count was used and the count made in the same way. A high dry (DD Zeiss) lens was used. By this method the red cells are not hemolyzed, but the basophilic granules appear as a purplish reticulum (Table 2).

3. The third method was to stain the blood vitally with a 5 per cent. aqueous solution of brilliant cresyl blue. A drop of blood is placed on a slide, a drop of stain added and the two mixed. A cover slip is put on and the edges sealed with celloidin to prevent drying. The slide is then placed on a warming stage and studied under high magnification. By this method the granules appear in large clumps with some fine reticular threads between, mostly aggregated toward the center of the cells. After five minutes few reticulated cells are generally seen. After fifteen minutes the reticulated cells are numerous. The erythrocytes are not hemolyzed. The leukocytes are only partially stained.

RESULTS

In the blood of the normal adult, the number of basophilic granular cells averages one to every two or three oil immersion fields.

Blood smears of full-term infants, taken during the first twenty-four hours of life, show a large number of basophilic granular cells.

This number decreases steadily and rather uniformly, so that by the eighth to the tenth day of life the basophilic cells are found in about the number as seen in adult normal life.

TABLE 2.—*Quantitative Estimation of Basophilic Cells to the Cubic Centimeter of Blood in the New-Born. Blood Pipet and Counting Chamber. Polychrome Methylene Blue*

Sex *	Color	Age	Date and Count									
♀	W	1 hour	2/ 6/25—18,000	2/ 7/25—16,400	2/ 9/25—14,000	2/10/25—11,200	2/12/25—6,000	2/13—4,300	2/14—1,200	2/16—250	2/17—20	
♂	C	12 hours.	2/ 9/25—16,000	2/10 —14,000	2/11 — 9,400	2/12 — 8,800	2/13 —4,200	2/14—2,000	2/16— 270	2/17—130	2/18—25	
♀	W	12 hours.....	2/16/25—16,400	2/17 —14,000	2/18 —11,200	2/19 — 7,000	2/20 —4,800	2/21—2,000	2/23— 750	2/24— 10		
♂	W	18 hours.....	2/17/25—17,000	2/18 —15,000	2/19 —12,800	2/20 — 9,400	2/21 —6,400	2/23—2,000	2/24— 450	2/25— 10		
♂	W	6 hours.....	3/ 9/25—17,000	3/11 —14,400	3/13 —11,000	3/16 — 4,200	3/18 —1,000	3/20— 20	Twins			
♂	W	6 hours.....	3/ 9/25—15,800	3/11 —13,800	3/13 —10,800	3/16 — 3,200	3/18 — 450	3/20— 10				
♂	C	12 hours.....	3/16/25—14,800	3/18 —10,000	3/20 — 4,000	3/23 — 250	3/25 — 10					
♂	W	7 months.....	3/16/25—28,400	3/18 —20,400	3/20 —16,000	3/21—Child died						

Premature, 12 hours after birth

* In this column, ♀ indicates female; ♂ male.

Tables 1 and 2 show the incidence and the decrease graphically. Table 1 is a study of cases by the approximate method of McCord. Table 2 shows the results of our own method of more accurate counts.

The blood of premature infants shows a somewhat higher percentage of basophilic cells than does the blood of infants born at term, but the rate of decrease approximates that of the normal infant (see last case, Table 2).

A smear of the blood of a 3 cm. fetus showed approximately 50 per cent. of nucleated red cells. Stained with polychrome methylene blue, the cytoplasm of all the erythrocytes was stained more heavily than would be normal for the new-born, but no definite granules could be made out.

Finally, we have made a comparison of the blood of the new-born, using three different stains on three smears taken at the same time.

Ordinarily, Wright's stain shows simple polychromatophilia without definite stippling. Smears stained with methylene blue showed fairly large basophilic granules, which tended to aggregate at the periphery of the cells, giving a definite ring formation. Stained with polychrome methylene blue or with brilliant cresyl blue—the basophilic granules appeared smaller—fairly evenly distributed throughout the cells, at times joined by fine threads.

In a series of cases of lead poisoning and severe anemias (not in infants), we found that the smears stained with polychrome methylene blue showed very large heavy granules stained with Wright's stain, smears of the same blood showed the ordinary stippling.

By the quantitative method, the number of basophilic cells in the blood of the new-born was found to be between 15,000 and 18,000 per cubic millimeter, and to decrease uniformly until by the tenth day the normal for adult blood had been reached.

BLOOD PLATELET COUNTS IN INFANTS AND IN YOUNG CHILDREN *

STAFFORD McLEAN, M.D.
AND
JOHN P. CAFFEY, M.D.
WITH THE TECHNICAL ASSISTANCE OF
KATHERINE V. KREIDEL, A.B.
REBECCA BURLAND, A.B.
AND
MABEL BROD
NEW YORK

The first careful studies of the platelets were made by Max Schultze [1] in 1865, but to Wright [2] belongs the credit for our present exact knowledge of their origin. He demonstrated the ability of the megakaryocytes to throw pseudopodia into the sinuses of the bone marrow, and produced the present quite generally accepted evidence that these cytoplasmic processes becoming detached from the parent cell are carried in the blood as the platelets.

Ledingham,[3] in 1914, confirmed Wright's findings and demonstrated the existence of the platelets as entities by preparing an antiserum with guinea-pig platelets as antigen, which was capable of destroying the platelets of the same species on parenteral injection. Bedson [4] not only verified this observation, but showed that the disappearance of the platelets from the blood of the injected guinea-pig is followed by severe purpura.

Dyke [5] states that there can be no doubt the platelets are entities, and that the proof is now complete of their relationship to the hemorrhagic diathesis and to the production of purpura. He mentions that Duke has shown that when the platelet count falls below 60,000 per cubic millimeter there is an abnormal tendency to bleed; that when it falls below 10,000 hemorrhage becomes severe and when below 1,000, fulminant. Bedson [6] states that experimental evidence has been brought forward to show that the two main factors concerned in the production

* Received for publication, Aug. 8, 1925.

* From the Babies Hospital.

* Read before the Section on Diseases of Children at the Seventy-Sixth Annual Session of the American Medical Association, Atlantic City, May, 1925.

1. Wright, J. H.: Nelson Living Medicine **4**:5.

2. Wright, J. H., and Kinnicutt, R.: A New Method of Counting the Blood Platelets for Clinical Purposes, J. A. M. A. **56**:1457 (May 20) 1911.

3. Ledingham, J. C. L.: Lancet **1**:1673, 1914.

4. Bedson, S. P.: J. Pathol. & Bacteriol. **25**:94 (Jan.) 1922.

5. Dyke, S. C.: Lancet **2**:714 (Oct. 4) 1924.

6. Bedson, S. P.: Footnote 4.

of hemorrhage are: (1) Toxic action on the endothelium of the vessels, and (2) removal of the platelets from the circulation.

Frank [7] recognized three degrees of primary disease of the bone marrow and endeavored to correlate, as follows, all the forms of purpura associated with thrombopenia.

Intermittent Thrombopenia.—This condition, occurring mainly in children, manifests itself clinically by occasional recurrent attacks of hemorrhage and purpura, and embraces those conditions now variously known as purpura hemorrhagica, pelios rheumatica, Henoch's purpura, etc. Prior to the onset of the hemorrhagic manifestations in these patients, there is always a diminished platelet count. Between attacks it is normal, with some degree of leukopenia and with an actual and relative decrease of the polymorphonuclears.

Essential Thrombopenia.—This is characterized by its intermittency and by a tendency to disappear. In certain individuals it may last for long periods or throughout life. These patients bruise easily and may at times have attacks of purpura or hemorrhage of varying degree of severity. The blood picture shows anemia, a reduction in the platelet count, leukopenia of varying degree, and a diminution in the polymorphonuclear neutrophils, both relative and absolute.

Aleukia Hemorrhagica or Aplastic Anemia.—This is an accentuation of the before-described features. There is severe anemia, reduction of the platelets, reduction of the granular leukocytes, purpura and hemorrhage. In the most severe cases the hemorrhage may be intense and the disease becomes rapidly fatal. All three forms are believed by Frank to be due to a primary deficiency of the bone marrow.

Dyke mentions that enlargement of the spleen is a feature of all three types, and that such spleens on histologic examination frequently show masses of platelets in the sinuses. Bedson has demonstrated the thrombocytolytic action of the spleen, showing that in the guinea-pig splenectomy is followed by a great but temporary rise in the platelet count, but that the count soon reverts to a normal level.

Crawford's [8] studies regarding the platelets in relation to the bone marrow tends to show that the platelets are increased when the bone marrow is active, and diminished when the contrary is the case. Thus, in the myeloid types of leukemia, a great excess of granular leukocytes is associated with an intense thrombocytosis, while in the lymphatic type the platelets are considerably decreased. Crawford mentions that F. Moller was able to produce typical purpura hemorrhagica with a marked fall in the platelet count by exposing guinea-pigs to the roentgen ray.

7. Frank, quoted by Dyke, S. C.: Lancet **1**:1051 (May 24) 1924.
8. Crawford, G. J.: Lancet **2**:595 (Sept. 20) 1924.

NORMAL PLATELET COUNT

There is no unanimity of opinion as to what constitutes a normal platelet count for adults, but it is generally agreed that the count varies normally more than the count of red and white cells. Duke [9] believes that the platelets are short lived bodies, thus accounting for the fact that the count can rise and fall with such rapidity and that they are utilized and regenerated in enormous numbers daily.

Gram [10] states that various authors have estimated the normal platelet count as between 200,000 to 800,000 per cubic millimeter, nearly all agreeing that the boundary lines of the normal must be rather widely separated. Wright and Kinnicutt [11] found that the platelet count of normal adults varies between 226,000 and 367,000 with a general average of 297,000. They quote the figures of Pizzini as from 250,000 to 370,000; of Determan, from 180,000 to 250,000; of Cadwalder, from 259,000 to 400,000 and of Pratt, from 226,000 to 377,000, but they refuse to accept the figures of some eighteen other observers with counts from 416,000 to 725,000.

Reimann [12] mentions figures of other investigators which give 200,000 to 850,000 as normal counts for adults, but, using Olaf Thomsen's method, his own studies gave a normal of 350,000 with only slight variations from time to time.

Lucas and Fleischner [13] in Abt's "Pediatrics" give the normal for children as 250,000, with variations from 200,000 to 400,000. Crawford mentions that the counts in children may be higher than in adults.

Variations from the Normal Platelet Count.—It is generally agreed that the platelets are diminished in genuine idiopathic purpura, in pernicious anemia and in acute lymphatic anemia, and are increased after hemorrhage and greatly increased after severe hemorrhage.

In addition to these generally accepted variations in the platelet count, other evidence of platelet reaction has been presented.

Wright and Kinnicutt found that in secondary anemia the platelet count was usually increased. In typhoid fever during the early stages, these authors observed a decrease in the number of platelets, with an increasing number as the disease advanced and with very high counts during convalescence. Bannermann [14] mentions that in tuberculosis there is

9. Duke, W. W.: Causes of Variation in the Platelet Count, Arch. Int. Med. **11**:100 (Jan.) 1913.

10. Gram, H. C.: On the Platelet Count and Bleeding Time in Disease of the Blood, Arch. Int. Med. **25**:325 (March) 1920.

11. Wright, J. H., and Kinnicutt, R.: Footnote 2.

12. Reimann, H. A.: J. Exper. Med. **40**:553 (Oct.) 1924.

13. Lucas and Fleischner: Abt's Pediatrics, Philadelphia, W. B. Saunders Company **4**:423.

14. Bannermann, R. G.: Lancet **2**:593 (Sept. 20) 1924.

a tendency to a thrombocytosis, and that, in general, the more advanced is the disease the greater is the degree of thrombocytosis.

During acute infection, Reimann observed that the platelets are decreased, while during convalescence they become normal or higher than normal. Both Reimann and Wright and Kinnicutt found that at or soon after the crisis of acute lobar pneumonia, the platelets increase with great rapidity. Wright and Kinnicutt found that during the acute stages the platelets may be low, normal or slightly above normal, while Reimann noted that a thrombopenia occurred during the fever and a subsequent thrombocytosis after the temperature became normal. Most of Crawford's smaller group of cases of bronchopneumonia in children showed a platelet increase, but one showed a definite fall.

Gullard and Goodall [15] found the platelets to be decreased in infectious disease during the febrile stage, with the exception of scarlet fever. The same authors found the platelets to be decreased in scurvy, cachexia and malnutrition, and increased in secondary anemia in most inflammatory and septic conditions and after injection of antiserums.

Lucas and Fleischner noted an increase during most inflammatory and septic conditions. Bannermann states that Cramer, Drew and Mottram found that thrombopenia could be induced by vitamin A starvation or by appropriate exposure to radium or to the roentgen ray. Duke found that following tuberculin injection the platelets increased in number, and that very striking increases occurred after large doses of tuberculin.

METHOD

Before commencing this study, the four following methods of counting blood platelets were given a thorough trial: Gram's [16] modification of Olaf Thomsen's, Buckman and Hallisey's; [17] Wood, Vogel and Famulener's [18] staining with brilliant cresyl blue, and Wood, Vogel and Famulener's sodium citrate method.

These four methods gave consistent results, but the last named was selected as the method of choice because of its simplicity. In addition, it requires no elaborate preparation of solutions, the platelets can be expeditiously and accurately determined with a minimum of equipment, and coincident counts of red cells and platelets can be made in the same counting chamber.

The blood was drawn to the 0.5 mark in the red pipet, and diluted to 101 with 3 per cent. sodium citrate solution. Three grams of chem-

15. Gullard and Goodall: New York, E. B. Treat, 1925, p. 97.
16. Gram, H. C.: Footnote 10.
17. Buckman, T. E., and Hallisey, J. E.: Studies in the Properties of Blood Platelets, J. A. M. A. **76**:427 (Feb. 12) 1921.
18. Wood, Vogel and Famulener: Laboratory Technique, New York, J. T. Dougherty, 1922.

ically pure sodium citrate to 100 c.c. of freshly distilled water, and filtered when required, is used. Five cubic centimeters of this solution was put in sterile Wassermann tubes, autoclaved for twenty minutes at 20 pounds pressure and then kept on ice until used. A fresh 5 c.c. tube of sodium citrate solution was used for each count. The pipet was shaken for three minutes and after expelling the first 3 drops, the next was put on the counting chamber with Turk ruling. Ordinary cover glass was used. Red blood cell count was then made, and at the end of approximately five minutes the platelets had settled out sufficiently for counting.

In most instances, the blood was obtained from the finger, sometimes from the heel and occasionally from a vein of the neck or the arm.

PLATELET COUNTS IN NORMAL INFANTS AND CHILDREN

New-Born Infants.—These counts were made in fifteen new-born infants.[19]

TABLE 1.—*New-Born Infants*

Age. Hours	Red Blood Cells	White Blood Cells	Platelets
5	5,504,000	18,100	224,000
7	5,800,000	24,400	360,000
12	5,280,000	17,000	240,000
14	5,000,000	15,010	216,000
24	6,000,000	18,000	264,000
24	4,480,000	14,200	280,000
24	5,900,000	17,600	264,000
29	6,800,000	16,900	288,000
48	4,350,000	16,600	276,000
72	5,300,000	8,800	328,000
72	5,100,000	6,200	232,000
96	6,700,000	4,400	232,000
120	5,072,000	16,400	320,000
120	3,500,000	7,600	320,000
120	4,900,000	7,100	320,000

The count of the youngest infant of this group was done five hours after birth; in two, from six to twelve hours after birth; in two, from twelve to twenty-four hours after birth. Of the remaining ten infants, none was more than 5 days of age. The average count for this group was 278,000 per cubic millimeter. The lowest count was 216,000, and the highest was 360,000.

The red blood cell counts in these fifteen infants, as would be expected, generally exceeded 5,000,000; three were more than 6,000,000 (Table 1).

Premature Infants.—This group includes ten premature infants from 2 days to 9 weeks of age. The average count was 246,000. The lowest count of 152,000 was found in an infant, aged 63 days, and the highest

19. The platelet counts in the new-born were made at the Manhattan Maternity Hospital, through the courtesy of Dr. Frederick W. Rice.

358,000 in an infant, aged 7 days. As noted in the table, there was no relationship between the number of red cells or white cells and the platelets. An infant with 5,664,000 red blood cells had only 176,000 platelets, while another with 3,900,000 showed 340,000 platelets. The absence of relationship between the white blood cells and the platelets is illustrated by a platelet count of 358,000 with 7,900 white blood cells in one infant, and a platelet count of 176,000 with 7,500 white blood cells in another (Table 2).

TABLE 2.—*Premature Infants*

Age, Days	Hemoglobin	Red Blood Cells	White Blood Cells	Platelets
2	115	4,900,000	18,500	272,000
4	110	5,400,000	12,000	176,000
7	115	6,600,000	7,900	358,000
15	105	6,016,000	8,900	240,000
19	100	4,768,000	13,800	320,000
20	110	5,700,000	7,500	176,000
21	100	5,500,000	9,340	208,000
39	110	4,900,000	9,340	216,000
63	90	3,300,000	7,950	152,000
63	70	3,900,000	10,800	344,000

TABLE 3.—*Infancy*

Age	Hemoglobin	Red Blood Cells	White Blood Cells	Platelets
3 weeks	...	5,400,000	.....	392,000
6 weeks	120	5,200,000	36,300	296,000
7 weeks	...	4,400,000	.....	336,000
2 months	85	4,400,000	6,900	464,000
2 months	75	3,900,000	5,700	568,000
2 months	85	3,600,000	7,600	304,000
9 weeks	75	3,500,000	14,000	272,000
10 weeks	...	3,104,000	7,900	280,000
3 months	70	3,800,000	17,500	292,000
3 months	60	3,600,000	20,000	368,000
5 months	75	4,200,000	7,600	304,000
6 months	70	4,062,000	7,800	272,000
6 months	75	3,400,000	3,450	288,000
6 months	85	4,800,000	13,900	408,000
7 months	...	5,824,000	.....	516,000
8 months	80	5,450,000	15,600	416,000
12 months	80	4,600,000	11,000	328,000

Infancy.—The following seventeen infants, aged from 3 weeks to 1 year, were discharged from the hospital with the note that they had no demonstrable pathologic condition. These infants were admitted either for social reasons or for dietetic regulation, and while in the hospital were free from symptoms. The lowest platelet count was 272,000 and the highest 568,000. The average count for the nineteen infants was 359,000.

As in the premature and new-born groups, there was no apparent relationship between the platelets and the other formed elements of the blood (Table 3).

Early Childhood.—Platelet counts were determined in nine normal children from 1 to 6½ years of age. The counts varied from 216,000 to 528,000 with an average of 341,000 (Table 4).

On reviewing the before-mentioned four groups, it is notable that the number of platelets in the first two groups, namely, the new-born and the premature infants, averaged 278,000 and 246,000, as contrasted with an average of 359,000 and 346,000 in the two older groups of infancy and of early childhood. These findings would seem to demonstrate that the number of platelets in the new-born and premature infants tend to be somewhat lower than in infants and older children.

TABLE 4.—*Early Childhood*

Age	Hemoglobin	Red Blood Cells	White Blood Cells	Platelets
13 months	80	5,100,000	19,700	336,000
22 months	62	5,024,000	11,800	440,000
24 months	80	4,390,000	7,000	528,000
2½ years	75	5,400,000	12,200	336,000
3 years	75	3,690,000	8,200	216,000
3½ years	90	4,780,000	22,400	264,000
3 years	75	4,490,000	16,950	304,000
4½ years	80	4,900,000	12,200	368,000
6½ years	80	4,080,000	6,800	280,000

TABLE 5.—*Anemia*

Diagnosis	Age	Hemoglobin	Red Blood Cells	White Blood Cells	Platelets	Polymorphonuclears	Lymphocytes	Mononuclears
Congenital syphilis..	3 mos.	40	3,100,000	9,800	384,000	..	..	..
Cong. mal. of heart.	2 mos.	35	2,100,000	17,000	88,000	45	45	5
Secondary anemia...	12 mos.	30	952,000	7,600	104,000	62	37	1
Secondary anemia...	17 mos.	20	1,500,000	35,000	208,000	87	6	3
Status lymphaticus..	22 mos.	25	1,000,000	40,000	336,000	61	31	5
Scurvy	9 mos.	25	1,490,000	7,200	232,000	60	32	2
Secondary anemia...	32 mos.	40	2,300,000	9,700	184,000	61	29	6
Sepsis, jaundice.....	7 wks.	40	1,600,000	13,000	184,000	45	48	3
Pyelonephritis	11 mos.	39	3,700,000	12,000	272,000	72	27	1
Acute bronchitis.....	17 mos.	40	3,000,000	12,600	600,000	51	45	4
Pyopneumothorax ..	18 mos.	35	3,100,000	12,000	184,000	57	33	8
Bronchopneumonia .	13 mos.	35	2,900,000	16,000	112,000	44	52	1
Suppurative Pleurisy	15 mos.	40	3,800,000	15,000	472,000	77	21	1
Bronchopneumonia .	21 mos.	40	2,800,000	10,400	376,000	..	..	..

There is also a tendency for the counts in premature and new-born infants to remain within narrower limits than in infancy and early childhood. In infancy and early childhood, the tables show a much wider variation. In the two younger groups the platelets fluctuated between limits of approximately 100,000, while the fluctuation in the older groups was nearer 300,000.

DISEASES OF THE BLOOD

Anemia.—Platelet counts were made in fourteen cases of anemia, none of which was due to hemorrhage. The anemia was the only factor considered in the grouping of these cases (Table 5).

In fourteen patients with anemia, aged from 7 weeks to 32 months, the average hemoglobin estimation was 34 per cent., the average red cell count was 2,400,000 and the average platelet count was 266,000. In two cases the platelets were diminished below the limits of normal, while in the balance they were within the range of normal. A comparison of the hemoglobin percentage with the number of platelets reveals no parallelism, which is also true in a comparison of the red cells with the platelets.

In four patients with severe anemia with enlargement of the spleen, splenectomy was performed (Table 6). These cases could not be classified in any of the accepted types of anemia. None of the patients showed purpura or bleeding from the mucous membranes.

TABLE 6.—*Splenectomy Cases*

	Before Operation					
	20 Weeks	16 Weeks	12 Weeks	8 Weeks	4 Weeks	1 Week
Case 1	.....	208,000	288,000	192,000	.....	216,000
Case 2	.....	.....	.....	.....	.....	.....
Case 3	116,000	.....	96,000	184,000	144,000	128,000
Case 4	.....	.....	.....	324,000	192,000	100,000

	After Operation							
	1 Week	4 Weeks	8 Weeks	12 Weeks	16 Weeks	8 Months	20 Months	44 Months
Case 1	192,000	.....	184,000	328,000	.....	.....	.....	.....
Case 2	.....	.....	.....	.....	.....	.....	515,000	592,000
Case 3	192,000	184,000	272,000	200,000	.....	384,000	.....	.....
Case 4	192,000	192,000	240.000	184,000	368,000	.....	.....	.....

REPORT OF CASES

CASE 1.—C. M., a girl, aged 3 years, was admitted to hospital because of fever and pallor for one month.

Physical examination showed a moderately well nourished child, not acutely ill, with a large hard spleen, the lower pole of which was 3 inches below the costal margin. The Wassermann blood test was 4 plus; of the spinal fluid it was negative. The blood examinations indicated a severe anemia, with normal platelets and a few nucleated red cells. Treatment with neoarsphenamin and mercury caused no improvement. Grossly and microscopically, the spleen showed marked perisplenitis and interstitial splenitis, syphilitic in type.

CASE 2.—S. G., a boy, aged 4 years, was admitted to hospital with a history of pallor and weakness which began in infancy. Examination showed a marked pallor with lemon tint to the skin, and a large hard spleen which extended below the umbilicus. The Wassermann test of the blood was negative. The blood gave the picture of an anemia with no distinctive features. The red cells showed a normal degree of hemolytic fragility. The spleen showed marked congestion and a moderate, early fibrosis. The platelets, after operation, reached the highest zone of the normal.

CASE 3.—B. S., a girl, aged 2 years, was admitted to hospital because of pallor and loss of weight of four months duration. Examination showed marked pallor with a yellowish tint to the skin, a protuberant abdomen with an enlarged spleen extending to the level of the umbilicus, and a liver extending three finger breadths below the costal margin. The Wassermann test of the blood was nega-

tive. This patient is one of a family of seven children, three of whom have had splenectomies performed because of an enlarged spleen, liver and marked anemia.

CASE 4.—N. S., a boy, aged 11½ months, a brother of the patient described in Case 3, was admitted because of pallor of three weeks duration, and progressive enlargement of the abdomen for the same period. Examination showed pallor, a liver three finger breadths below the costal margin, and a spleen which extended one finger breadth below the umbilicus.

Cases 3 and 4 were brother and sister, suffering from a familial blood dyscrasia characterized by a severe anemia, with a normal leukocytic count and a few nucleated red cells. After splenectomy, there was a mononucleosis extending over several months. The platelets remained unchanged.

Microscopic examination of the spleen showed a more marked fibrosis with congestion in the younger child, and no change in the malphigian bodies.

Comment.—In four cases of splenectomy there was an increase in the number of platelets following the operation.

TABLE 7.—*Leukemia*

Case 1.—A. F.							
Date	Hemoglobin	Red Blood Cells	White Blood Cells	Platelets	Polymorphonuclears %	Lymphocytes %	
Sept. 4....	25	1,500,000	7,200	88,000	15	80	Transfusion 180 c.c. whole blood
Sept. 5....	50	2,000,000	7,800	104,000	3	84	
Sept. 9....	45	2,200,000	6,100	.....	6	81	
Sept. 13....	45	1,500,000	1,700	200,000	11	86	
Sept. 15....	45	1,500,000	1,750	.....	4	86	
Sept. 17....	35	1,600,000	1,850	208,000	8	82	
Sept. 22....	30	1,100,000	1,600	128,000	23	73	
Sept. 29....	25	992,000	3,600	120,000	38	58	
Oct. 2.....	30	1,080,000	4,400	120,000	33	61	
Oct. 3.....	..	.....	.....	.....	..	..	Blood transfusion
Oct. 6.....	50	2,500,000	2,900	157,000	45	54	
Oct. 10.....	70	2,300,000	3,600	168,000	28	67	
Oct. 17.....	75	4,800,000	6,800	228,000	33	59	
Nov. 7.....	60	3,600,000	4,600	176,000	2	92	
Nov. 20.....	55	3,200,000	3,500	168,000	7	85	
Dec. 1.....	45	2,080,000	3,700	192,000	21	66	Coagulation time, 4 minutes
Dec. 8.....	44	2,000,000	5,200	112,000	8	89	
Dec. 13.....	..	.....	.....	.....	..	..	Transfusion, 150 c.c.
Dec. 15.....	52	2,500,000	6,150	144,000	3	73	
Dec. 18.....	40	2,200,000	3,600	.....	9	84	

In all four patients, the nucleated red cells were increased after splenectomy, and in two mononucleosis also appeared. The independence of blood platelet production and the production of other myelogenous elements, the polymorphonuclear leukocytes and red blood cells, would seem to be upheld by these observations.

The three following cases will be considered together on account of the similarity of the blood picture. All were patients with acute lymphatic leukemia, and one showed marked involvement in the thymus gland in the leukemic infiltration process.

CASE 1.—A. F., aged 15 months, was admitted because of pallor from birth and weakness of three weeks duration. This patient was under observation for a period of three and one-half months. During this period, fifteen blood examinations were made, the last, five days prior to death (Table 7).

Throughout the period of observation, fine subcutaneous hemorrhages and large areas of ecchymosis were observed, but there was no bleeding from the mucous membranes. The spleen remained large. The average platelet count of fifteen examinations was 154,000, which, according to our observations, is definitely below the normal for the age group to which this child belongs, which is 336,000.

Each of three transfusions was followed by a moderate increase in hemoglobin, red blood cells and platelets. The white cells were not influenced by transfusion, remaining consistently low with only six counts showing more than 5,000. The diagnosis of an aleukemic leukemia was made on the decreased total white count with high lymphocytic percentages in the differential. The patient died five days after the last count following the development of suppurative parotitis.

CASE 2.—P. P., a girl, white, aged 8½ months, with acute lymphatic leukemia, had had repeated subcutaneous hemorrhages of face, hands and feet since the age of 5½ months. She was under observation for a period of three days. It was subsequently learned that she died at home (Table 8).

Examination showed a purpuric eruption of variable size, limited to the face, hands and feet. The cervical, axillary, epitrochlear and inguinal glands, as well as the spleen and liver, were definitely enlarged. There were no hemorrhages from the mucous membranes. The platelet counts in this case were definitely below the normal, with an average for the two counts of 100,000.

TABLE 8.—*Leukemia*

	Case 2.—P. P.								
Date	Hemoglobin	Red Blood Cells	White Blood Cells	Platelets	Polymorphonuclears	Lymphocytes	Mononuclears	Myeloblasts	Transitionals
Nov. 14...	50	2,600,000	50,200	96,000	6	49	18	24	3
Nov. 17...	50	2,400,000	77,500	104,000	1	85	0	14	0

CASE 3.—P. P., a girl, white, aged 2½ years, was admitted to the hospital because of puffiness of the eyes of two months duration and brownish discoloration of the skin for eight days. Examination showed a purpuric eruption on the legs and chest, ecchymosis under the eyes and a larger subcutaneous hemorrhage of the frontal region. The spleen was not palpable.

During the period of observation, epistaxis occurred, bloody vomitus on several occasions and blood was passed with the stool.

Necropsy revealed an enlarged thymus and mediastinal lymph nodes with metastases in spleen, kidney and liver, and subcutaneous, subserous and subperitoneal hemorrhages. The final diagnosis in this case was thymic leukemia. The average platelet count for nine examinations was 147,000 (Table 9).

The average platelet count in each of three cases, namely, 154,000, 100,000 and 147,000, shows a definite reduction as compared with 351,000 and 336,000 for the age groups to which they belonged.

CONGENITAL MALFORMATIONS OF HEART

This group is represented by four patients varying from 1 day to 11 months of age (Table 10). The platelet count in each is normal, and the four lie within the narrow range of 335,000 to 372,000. The lack of relationship between the platelet count and the red blood cell count is shown in this group, the red blood cells of which vary from 2,700,000 to 6,360,000, while the platelets remain practically constant at about 350,000 (from 335,000 to 372,000).

RESPIRATORY DISEASES

Acute Bronchitis.—Platelet counts were made on ten infants with acute bronchitis, aged from 1 month to 3 years of age. The average count for the ten cases was 352,000. The lowest platelet count was 192,000 in an infant aged 10 months, with a complicating tetany. The highest count of 600,000 was noted in a child, aged 17 months, with a complicating otitis media and a definite blood picture of secondary anemia. The red cells numbered 3,048,000 and the hemoglobin percentage was 40.

TABLE 9.—*Leukemia*

	Case 3.—P. P.					
Dates	Hemoglobin	Red Blood Cells	White Blood Cells	Polymorphonuclears	Lymphocytes	Platelets	
April 25	40	1,800,000	9,450	1	99	.....	
April 25	..	.....	.....	..	..	.....	Transfusion 230 c.c. whole blood
April 26	65	3,400,000	7,500	4	89	.....	
April 30	50	2,200,000	1,200	23	66	52,000	
June 3	40	2,300,000	7,500	3	96	52,000	
June 5	..	.....	.....	..	..	.....	Transfusion 160 c.c.
June 6	60	2,800,000	71,000	6	94	334,000	
June 12	..	.....	.....	..	..	.....	Transfusion 200 c.c.
June 14	60	2,500,000	42,000	2	97	192,000	
June 19	50	2,700,000	34,400	6	89	64,000	
June 20	50	2,700,000	50,400	2	98	224,000	Coagulation time 2½ minutes
June 24	..	.....	.....	..	..	.....	Transfusion 200 c.c.
June 26	35	1,400,000	7,450	6	91	200,000	
July 3	35	1,004.000	5,700	28	68	—	
July 8	..	.....	.....	..	..	.....	Transfusion 200 c.c.
July 9	60	2,600,000	39,000	32	65	160,000	
July 16	40	1,900,000	75,000	6	94	44,000	
July 18	Died						

TABLE 10.—*Congenital Malformation of Heart*

Age	Hemoglobin	Red Blood Cells	White Blood Cells	Platelets	Polymorphonuclears	Lymphocytes	Mononuclears
1 day.....	70	2,750,000	15,900	344,000	61	39	2
3 weeks.....	100	5,500,000	7,500	372,000	—	—	—
10 months.....	120	6,360,000	16,800	360,000	55	38	4
11 months.....	70	4,300,000	17,200	366,000	60	34	4

Pneumonia.—Platelet counts were made on a large number of infants and young children with acute infections. The largest single group was bronchopneumonia. In the few patients showing lobar pneumonia at necropsy, bronchopneumonia was also noted either in the same lung or on the opposite side. The diagnosis was established by the clinical signs with the aid of the roentgen ray, or by necropsy.

The youngest patient was 4 days of age, and the oldest was 5 years. The lowest count was 112,000 and the highest 752,000 with an average for the sixty-nine cases of 328,000 per cubic millimeter. Three had platelet counts of less than 200,000, one of which with a count of 128,000 showed an extensive petechial eruption of the trunk and extremities.

At necropsy, small multiple abscesses of the lungs and a catarrhal colitis were found. Sixty-two patients showed platelet counts between 200,000 and 500,000, and in only four were there more than 600,000 platelets.

The lowest count, 112,000, was noted in an infant with bronchopneumonia, who had marked anemia. The hemoglobin was 35 per cent. and the red cells were 2,900,000.

Acute Suppurative Pleurisy.—Platelet counts were made on sixteen patients with acute suppurative pleurisy, the youngest of whom was 3 months, and the oldest was 4 years. The average count for the group was 334,000, the lowest count was 216,000 and the highest count was 450,000. There were no unusual blood findings in any of these cases.

Pneumothorax and Pyopneumothorax.—Platelet counts were made in three cases of pyopneumothorax, and one of pneumothorax. The youngest was 4 weeks, and the oldest was 3 years of age. The average for the four cases was 338,000. The lowest count of 184,000 was found in a child with secondary anemia, having a hemoglobin of 35 per cent. and 3,100,000 red blood cells. The highest count occurred in a child with a normal blood picture.

Tuberculosis.—Six cases of tuberculosis in young children showed normal platelet counts with an average of 316,000. Both chronic pulmonary and acute miliary types are included in this list.

Whooping Cough.—Two patients with whooping cough, one aged 10 weeks and the other aged 12 months, showed normal platelet counts of 312,000 and 248,000. The first case showed a leukocytosis of 30,000 with a lymphocyte count of 71 per cent. The second patient had a leukocyte count of 44,000 with 70 per cent. lymphocytes.

Tonsillectomy.—Platelet counts were made on seven children, varying in age from 2 to 5 years, admitted for tonsillectomy. There was a small amount of hemorrhage following each operation. The platelet counts in each child before operation was within the range of normal, with an average of 320,000. On the day following operation the counts remained within normal limits and averaged 263,000. This shows a slight but definite reduction in the number of platelets, which is contrary to the experience of Gulland and Goodall, who state that the platelets are increased even after slight hemorrhage.

CONGENITAL SYPHILIS

Seven infants with congenital syphilis, aged from 1 to 17 months, are presented (Table 11). These children all presented clinical and serologic evidence of syphilis, with positive histories of syphilis in the family.

Five of the counts fell within the normal range of from 200,000 to 384,000. Of special interest is Case 5. The patient was admitted with

a history of continuous oozing of blood from umbilicus, hands and feet, of two weeks duration. Transfusion was performed immediately. There were no observations on the platelets before transfusion. After transfusion (twenty-four hours) the platelet count was 200,000. No improvement was noted following transfusion, the patient dying forty-eight hours afterward without cessation of bleeding. There was blood stained vomitus before death. The major part of the hemorrhage in this case was from desquamated palms and soles. The persistency of the hemorrhage with a normal platelet count is contrary to the picture of an early true purpura hemorrhagica. The onset during the third week, and the lack of improvement after transfusion is not consistent with hemorrhagic disease of the new-born. During the active hemorrhage, the clotting time was four minutes. The fragility test showed a normal range of hemolysis in saline solution. A reasonable assumption in this case is that the bleeding was probably due to some change in the blood vessels caused by the syphilitic infection. Necropsy showed

TABLE 11.—*Congenital Syphilis*

Number	Age, Months	Hemoglobin	Red Blood Cells	White Blood Cells	Platelets
1	4	65	3,008,000	13,200	344,000
2	3	40	3,100,000	9,800	380,000
3	1	75	3,600,000	31,000	284,000
4	1	35	1,300,000	27,600	67,000
5	1¼	70	3,490,000	30,000	200,000
6	7	20	1,500,000	35,000	208,000
7	2	35	2,100,000	17,700	88,000

the lesions of syphilis in the spleen and liver, but no lesions of the blood vessels were demonstrable.

Cases 4 and 7 showed marked diminution in platelets, 67,000 and 88,000 respectively. The former patient (Table 12) was admitted with a history of bleeding from nose and one great toe for five days. The blood picture was that of severe anemia. Hemoglobin was 35 per cent., the platelet count was 67,000, clotting time was twenty-two minutes and bleeding time was one hour plus. A transfusion of 70 c.c. of blood in this case stopped the hemorrhages from the mucous membranes and skin within two hours. The blood findings improved, with hemoglobin, 60 per cent.; platelet count, 112,000; clotting time, seven minutes and bleeding time five minutes. There were no further hemorrhages. The infant died thirty-six hours following the transfusion. The picture here is one of thrombopenia with associated congenital syphilis. This case suggests that syphilis may produce a reduction of platelets perhaps by a depressed activity of the megakaryocytes due to the action of a syphilitic toxin on these cells, or perhaps by an active spirochetosis of the bone marrow. Transfusion in this case was able to overcome such

depressant action sufficient to increase the platelets to 112,000, and bring about a cessation of hemorrhage with normal bleeding and clotting time.

Case 7 shows a low platelet count of 88,000 with normal bleeding and coagulation time. No hemorrhages were observed.

DISEASES OF THE NERVOUS SYSTEM

Meningitis.—Platelet counts were made in fifteen patients with meningitis, aged from 1 month to 3 years (Table 13). The diagnosis was established by the recovery of the organisms from the cerebrospinal

TABLE 12.—*Congenital Syphilis (Case 4)*

	Age, Months	Hemoglobin	Red Blood Cells	White Blood Cells	Platelets	Coagulation Time, Minutes	Bleeding Time, Minutes
	1	35	1,300,000	27,600	67,000	22	60+
14 hours after transfusion	1	60	2,500,000	58,000	112,000	7	5

TABLE 13.—*Meningitis*

Age, Months	Hemoglobin	Red Blood Cells	White Blood Cells	Platelets	Polymorphonuclears	Lymphocytes	Mononuclears
Tuberculous							
12	105	6,500,000	26,400	240,000	87	6	4
12	80	5,700,000	15,000	296,000	71	19	5
13	80	5,500,000	18,000	328,000	71	21	4
14	85	4,700,000	19,000	376,000	75	14	6
18	85	4,400,000	7,900	256,000	70	23	4
21	75	4,228,000	8,700	448,000	62	32	6
24	90	5,400,000	15,600	384,000	90	7	3
24	75	4,256,000	14,400	232,000	—	—	—
25	75	3,700,000	11,100	248,000	73	22	4
26	80	4,800,000	13,000	200,000	82	13	2
Meningococcus							
1	80	4,064,000	33,600	274,000	70	28	2
36	80	4,680,000	27,600	184,000	79	16	3
36	85	4,900,000	12,600	288,000	70	28	2
Pneumococcus							
24	50	2,300,000	16,000	334,000	83	17	..
Influenza							
24	65	3,400,000	12,600	208,000	80	15	4

fluid or by necropsy. In ten cases the tubercle bacillus was the causative organism, in three the meningococcus; one was caused by the pneumococcus and one by the influenza bacillus.

In the ten cases of tuberculous meningitis the average platelet count was 300,000. The lowest count was 200,000 and the highest 448,000. In the three cases of meningococcus meningitis the counts were 288,000, 274,000 and 184,000, the last mentioned case, a child, aged 3 years, with meningococcemia, showed a well marked purpuric eruption. The cases due to streptococcus and influenza organisms showed counts of 440,000 and 208,000, respectively.

In these four types of meningitis—tuberculous, meningococcal, pneumococcal and influenzal—the number of platelets was normal in every instance, and was not significantly altered in one case of meningococcal meningitis with extensive purpura.

Idiopathic Encephalitis.—Platelet counts were made on three patients with encephalitis lethargica (epidemic encephalitis), aged 6 months, 34 months and 38 months, who showed counts of 336,000, 272,000 and 416,000, respectively.

Brain Tumor.—In two cases of brain tumor diagnosed clinically, the platelet counts were 296,000 and 256,000.

Brain Abscess.—In one patient, aged 5 years, with brain abscess (proved at necropsy), the count was 216,000.

Poliomyelitis.—The counts in two patients with this disease, aged 5 weeks and 1 year, were 376,000 and 280,000, respectively.

DISEASES OF THE DIGESTIVE TRACT

Acute Intestinal Indigestion.—This group is represented by ten patients, varying in age from 7 weeks to 14 months. The platelet counts ranged from 329,000 to 184,000. There is no constant parallelism between platelets and age nor platelets and white blood cell count. The youngest and the oldest gave practically the same counts, and there is no regular relationship between low platelet count and low white cell count or high platelet count and high white cell count. The three cases which terminated fatally showed normal platelet counts.

Acute Intestinal Intoxication.—The platelets in twelve patients with acute intestinal intoxication were found to be within limits of 184,000 and 364,000. The difference in the platelet counts was not associated with coincident changes in the other formed blood elements, nor was the platelet count indicative of the severity of the disease or of prognostic value in the patients who died. Clinically, all of these patients presented severe dehydration. This did not result in any appreciable concentration of the platelets. It is interesting to note that Cases 24988 and 25291, in whom the red cell counts were increased to approximately six and six and one-half million, possibly due to blood concentration resulting from dehydration, had platelet counts of 192,000 and 344,000, which are within the normal range of this age group.

Acute Catarrhal Colitis.—In one case of acute catarrhal colitis the platelets numbered 280,000 on one occasion and twelve days later 200,000. The patient died five days later of bacteremia.

In the other case the initial platelet count was 192,000 and two days later was 208,000. The highest leukocyte count in these two instances was 12,000.

DEFICIENCY DISEASES

Scurvy.—Five cases of scurvy are presented with platelet determinations (Table 14). These counts were made in each instance during the active stage of the disease. The counts fall within normal limits of 440,000 to 216,000. Case 3 presents an interesting feature in that there was a longstanding hematuria, and on admission a secondary anemia, with red cells reduced to 1,470,000 and a hemoglobin of 25 per cent. The platelet count at this time was normal, 232,000. The patient responded quickly to therapy. After seven days the hemoglobin increased to 35 per cent., the red cell count to 1,600,000, while the platelet count remained practically the same. At the end of two weeks of treatment the hemoglobin had increased to 60 per cent., the red cells to 3,200,000 and the platelets again remained practically stationary at 240,000. This is another instance of the independence of the platelet count and the red blood cells. The white cells paralleled the platelets in this case with practically stationary counts of 7,200, 6,700 and 7,200.

TABLE 14.—*Scurvy*

Case	Age, Months	Hemoglobin	Red Blood Cells	White Blood Cells	Platelets	Polymorphonuclears	Lymphocytes	Mononuclears
1	10	80	4,700,000	16,200	240,000	60	35	2
2	8	65	3,080,000	9,300	440,000	30	61	5
3	9	25	1,470,000	7,200	232,000	60	38	2
	7 days later	35	1,600,000	6,700	216,000	27	72	1
	14 days later	60	3,200,000	7,200	240,000	30	54	12
4	10	60	3,700,000	14,500	432,000	59	34	5
5	12	70	4,100,000	24,200	248,000	60	37	2

Rickets.—Normal platelet counts were found in three infants with rickets, two of whom had a complicating tetany. The counts were 320,000, 312,000 and 240,000, respectively.

OTHER ACUTE INFECTIONS

Nephritis.—Platelet counts were made in eight patients with nephritis, aged from 11 months to 2½ years. The counts were all within normal range, the lowest being 272,000 and the highest 384,000. There was uniformity in the various counts with an average of 338,000.

Pyuria.—In five patients with pyuria, aged from 3½ to 13 months, all the counts were within the range of normal; the lowest was 192,000, the highest 320,000 and the average 248,000.

Septicemia.—In three patients with septicemia, aged 5 weeks, 4 and 7 months, the count showed 120,000, 224,000 and 296,000 respectively.

Endocarditis.—In two cases of acute endocarditis the platelet count was 440,000 and 280,000 respectively.

Otitis Media.—In seven patients with otitis media, varying in age from 9 weeks to 44 months, the lowest platelet count was 264,000, the highest 440,000 and the average 342,000.

Suppurative Lymphadenitis.—In seven patients with suppurative lymphadenitis, aged from 16 days to 6 years, which included patients with either axillary, femoral or retropharyngeal lymph gland involvement, the average count was 319,000, the lowest 248,000 and the highest 432,000.

Nonsuppurative Lymphadenitis.—Nine cases of nonsuppurative lymphadenitis showed platelet counts which were within normal limits. The patients of this group varied in age from 3 months to 5½ years. The lowest count was 208,000, the highest 528,000, and average for the nine cases was 352,000.

Suppurative Cellulitis.—In three children, aged from 11 months to 3 years, each with a deep abscess of soft parts, the counts were 280,000, 328,000 and 424,000 respectively.

Sixty-five platelet counts were made in the forty-one different diseases, all of which were within the range of normal except the count of 88,000 in the case of thyoma with a profuse petechial eruption which will be reported in detail subsequently.

SUMMARY

Four hundred platelet counts were made in 352 different infants and young children. Platelet counts in the new-born, in infancy and early childhood in forty-one showed a wide variation, fluctuating normally between approximate limits of 216,000 and 568,000.

The average count in fifteen new-born infants was 278,000; in seventeen normal infants was 359,000, and in nine normal young children was 341,000.

Platelet counts in ten premature infants showed an average of 246,000.

In fourteen cases of severe anemia in children less than 22 months of age, the average platelet count was 266,000. In these cases, a severe anemia was not accompanied by an abnormal platelet count except in three instances when it was definitely diminished.

In four cases of splenectomy, there was a slight increase in the number of platelets during a long period of observation following the operation.

In three cases of acute lymphatic leukemia, there was a marked reduction in the number of platelets.

Diseases of the Respiratory System.—In ten cases of acute bronchitis, the platetlet counts were normal with an average of 352,000.

In sixty-nine cases of pneumonia, the average platelet count was 328,000. Three patients showed counts of less than 200,000 and four had counts of more than 600,000. In sixteen cases of acute suppurative pleurisy, the average platelet count was 334,000.

In four patients with pneumothorax, three of whom had suppurative pleurisy, the average platelet count was 338,000. In six cases of tuberculosis the average platelet count was 316,000. Two patients with whooping cough had normal platelet counts.

TABLE 15.—*Miscellaneous Diseases*

Disease	Counts
Acute pharyngitis	200,000
Endocrine disturbance, unclassified type	176,000
Pyemia	284,000
Erysipelas	284,000
Dermatitis exfoliativa	504,000
Eczema	256,000
Furunculosis	264,000
Cellulitis of right thigh	320,000
Arthritis (2 cases)	334,000, 472,000
Acute follicular tonsillitis (2 cases)	296,000, 256,000
Hypertrophy of tonsils (2 cases)	288,000, 400,000
Granuloma of sublingual space	296,000
Atelectasis	392,000
Thymoma	88,000
Toxic psychosis	325,000
Toxic neuritis	336,000
Chorea	472,000
Chronic hydrocephalus	280,000
Idiocy (2 cases)	528,000, 240,000
Convulsions (idiopathic)	448,000
Lead poisoning (2 cases)	408,000, 284,000
Phosphorus poisoning	288,000
Osteogenesis imperfecta	323,000
Anorexia nervosa	264,000
Celiac disease	336,000
Malnutrition (4 cases) average	376,000
Hemangioma (3 cases) average	313,000
Intussusception (2 cases)	312,000, 480,000
Fistula in ano	328,000
Congenital malformations:	
Spina bifida (2 cases)	323,000, 480,000
Inguinal hernia	520,000
Harelip and cleft palate (2 cases)	512,000, 168,000
Hypertrophic stenosis of the pylorus (4 cases) average	282,000
Peritonitis (3 cases)	427,000, 504,000, 336,000
Chronic appendicitis	240,000
Cyst of the buttocks	288,000
Adenoma of kidney	336,000
Cephalohematoma	184,000
Abscess of left leg	328,000
Abscess of intercostal muscle	424,000
Otitis media, acute purulent (7 cases) average	342,000

In five cases of active infantile scurvy, the platelet count varied between normal limits of 216,000 and 440,000.

In fifteen cases of meningitis the platelet counts were normal. In eight cases of other inflammatory diseases of the central nervous system, the platelet counts were normal.

In forty-four cases with various types of acute infection, the platelet count was normal, excepting one count of 120,000 in a patient with septicemia.

In five of seven cases of congenital syphilis the platelet counts were normal. The platelet count in seven children following tonsillectomy was not significantly altered.

In twenty-four cases of acute intestinal indigestion, acute intestinal intoxication and acute catarrhal colitis, the platelet counts were normal.

CONCLUSIONS

1. The platelet counts in normal infants and children fluctuate between approximate limits of 200,000 to 550,000, with a general average of 349,000. The number of platelets in the new-born and in premature infants is fixed within narrower limits and has lower averages, 278,000 and 246,000 respectively. The platelet count in early life approximates the normal count in adults.

2. A reduction in the number of platelets occurred in only three of fourteen patients with severe anemia.

3. Removal of the spleen caused a slight increase in the platelet count.

4. The platelet count was definitely reduced in three cases of lymphatic leukemia.

5. In 173 cases of acute infection in infancy and early childhood, there was no significant alteration in the number of platelets.

6. In the pathologic conditions studied in this group of cases, estimation of the blood platelets was of no valuable diagnostic aid, except in cases of acute lymphatic leukemia.

DISCUSSION

DR. E. C. FLEISCHNER, San Francisco: I have nothing to add to this work except to express my appreciation of the amount of labor expended. I think when anyone in this Section presents a paper involving so much careful study, some mention should be made of the fact, to show that we appreciate the work which has been done.

DR. FRANK C. CAFFEY, Montgomery, Ala.: The blood platelet count in infants is of interest. It is considered that the blood forming tissues, including the bone marrow, may hyperfunction with increase of platelets. In the first few cases studied there was limitation. In early life the blood forming organs are very sensitive. In pathologic conditions the white cells and the red cells have wild fluctuations. I think this shows clearly the lack of relationship between the elements of the blood.

THE CARBOHYDRATE METABOLISM OF THE MARANTIC INFANT*

FREDERICK F. TISDALL, M.D. (TOR.)
T. G. H. DRAKE, M.B. (TOR.)
AND
ALAN BROWN, M.B. (TOR.)
TORONTO, CANADA

One of the great pediatric problems at the present time is the feeding and treatment of marantic infants. It is true that in recent years since the introduction of concentrated feedings, a much greater degree of success in the treatment of these infants has been obtained than was formerly the case. Quite frequently, however, in spite of the most rational feeding, some of these infants fail to gain in weight and this with no clinical evidence of a gastro-intestinal disturbance. The question arises: Is this inability to gain due to a defective absorption from the gastro-intestinal tract, or to some derangement of the general metabolism of the body?

DIGESTION AND ABSORPTION OF FOOD BY THE MARANTIC INFANT

It is well recognized clinically, that of the three organic constituents of the food, namely, fat, carbohydrate and protein, the fat is more apt to cause digestive disturbances in marantic infants than either of the other two. Therefore, we would naturally look to a defective absorption of this constituent as one of the causes of marasmus. A great deal of investigative work has been done in the study of this aspect of the problem. Courtney,[1] in 1911, found a somewhat lessened absorption of fat in marantic infants but, as she pointed out, the absorption was approximately normal in the infants with marasmus, in whom the condition was not complicated by diarrhea. The same statement applies to the figures reported by Utheim.[2] Hutchison,[3] and Fleming and Hutchison,[4] after extensive investigations and a critical review of the literature, came to the conclusion that "there is no defect in the power of atrophic

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* Read at the third annual meeting of the Canadian Society for the Study of Diseases of Children, Ottawa, Ont., June, 1925.
* From the Wards and Nutritional Research Laboratories of the Hospital for Sick Children, and the Sub-Department of Pediatrics, University of Toronto.

1. Courtney, A. M.: Studies on Infant Nutrition: 1. Metabolism in Chronic Malnutrition, Am. J. Dis. Child. **1**:321 (May) 1911.
2. Utheim, K.: J. Metabol. Res. **1**:803 (June) 1922.
3. Hutchison, H. S.: Quart. J. Med. **13**:277 (April 20) 1920.
4. Fleming, G. B., and Hutchison, H. S.: Quart. J. Med. **17**:339 (July) 1924.

infants to absorb fat." Quite recently, Parsons [5] found no abnormality in the ability of the marantic infant to absorb fat.

In regard to protein absorption, Courtney,[1] Utheim,[2] Fleming and Hutchison [4] and others have found no evidence of any defects in the ability of marantic infants to digest and absorb this constituent of the food.

It is much more difficult to answer definitely as to the ability of the marantic infant to digest and absorb carbohydrate. Talbot and Hill,[6] Utheim,[2] Parsons,[5] and Courtney [7] found that large amounts of carbohydrate can be fed to marantic infants without any appreciable amount appearing in the stools. The objection may be raised that a part of the ingested carbohydrate is fermented in the gastro-intestinal tract and thus lost. While this certainly occurs in many diarrheal cases, there is no evidence from the examination of the stools of marantic infants without diarrhea, that there is an excessive fermentation of carbohydrate and resultant production of organic acids.

On account of the frequency with which marantic infants develop gastro-intestinal disturbances, Fleming [8] believes that "failure of the gastro-intestinal tract to deal with carbohydrates satisfactorily, is an important factor in the production (and maintenance) of atrophy." In this connection, it is to be remembered that the resistance of marantic infants to infection is less than that of normal infants, and that parenteral infections frequently produce, or are accompanied by, diarrhea. In our experience, gastro-intestinal disturbances in marantic infants are almost invariably secondary to parenteral infections. A careful consideration of this aspect of the problem leads one to the conclusion that the development of diarrhea in marantic infants is probably not due to any inherent derangement of the functions of the gastro-intestinal tract.

In regard to the sugar tolerance curve obtained after the ingestion of glucose, Brown [9] found that "the curve is identical in the normal and undernourished child." This would indicate that there is no defect in the ability of marantic infants to absorb carbohydrate. It is known that the administration of carbohydrate stimulates the ability of the organism to remove glucose from the blood stream.[10] We determined the sugar tolerance curves on marantic infants after the intravenous injection of glucose. We then increased the carbohydrate content of their feeding

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5. Parsons, L. G.: Lancet **1**:687 (April 5); ibid., 793 (April 19) 1924.
6. Talbot, F. B., and Hill, L. W.: The Influence of Lactose on the Metabolism of an Infant, With Special Reference to Fat, Nitrogen and Ash, Am. J. Dis. Child. **8**:218 (Sept.) 1914.
7. Courtney, A. M.: Personal communication.
8. Fleming, G. B.: Quart. J. Med. **14**:171 (Jan.) 1921.
9. Brown, M. J.: Quart. J. Med. **18**:175 (Jan.) 1925.
10. Foster, G. L.: J. Biol. Chem. **55**:303 (Feb.) 1923. Traugott, C.: Klin. Wchnschr. **1**:2384, 1922.

from 8 to 16 per cent. and after a few days repeated the sugar tolerance curve. Almost invariably, the injected glucose was removed from the blood stream more rapidly after the infant had received the high carbohydrate diet than before.

Thus, there is no evidence that the marantic infant is not able to digest and absorb carbohydrate in a normal manner, provided no diarrhea is present. On the other hand, there is considerable indirect evidence that the marantic infant does digest and does absorb carbohydrate as readily as the normal infant.

THE AVERAGE CONCENTRATION OF THE FASTING BLOOD SUGAR IN MARANTIC INFANTS

In 1911, Cobliner [11] found that the concentration of blood sugar was less in marantic infants than in normal infants. Although his values on normal infants varied considerably, still the lowest was only 0.076 per cent., while in many marantic infants he found values as low as 0.050 per cent. He made the interesting observation in two atrophic infants that, as their condition improved, the concentration of blood sugar increased. A similar observation was made by Mogwitz.[12] In a recent article, Brown [9] reported a steady rise in the blood sugar of four marantic infants as the state of their nutrition improved. The last-mentioned author found an average fasting blood sugar of 0.077 per cent. in children whose actual weight was less than 50 per cent. of their expected weight, while in children whose actual weight was from 50 to 80 per cent. of their expected weight the average value was 0.091 per cent. As a result of these observations, she concluded that the level of the blood sugar bears a definite relationship to the degree of wasting. Guy [13] found the percentage of blood sugar in atrophic infants to be slightly lower than in normal infants.

We determined the fasting blood sugar in twenty-five marantic infants. The average value found was 0.076 per cent. as compared with the average value in normal infants of 0.085 per cent. It is quite apparent from a review of the literature and from our own figures that the concentration of the fasting blood sugar is lower in marantic infants than in normal infants.

HEAT PRODUCTION AND HEAT LOSS

The heat output of the marantic infants per kilogram of body weight has been found by Bahrdt and Edelstein,[14] Benedict and Talbot,[15] Murlin

11. Cobliner, S.: Ztschr. f. Kinderh. **1**:207, 1911.
12. Mogwitz: Monatschr. f. Kinderh. **12**:569, 1914.
13. Guy, R. A.: Quart. J. Med. **15**:9 (Oct.) 1921.
14. Bahrdt and Edelstein: Festschrift Dr. Otto L. Heubner, Berlin, 1913.
15. Benedict, F. G., and Talbot, F. B.: Carnegie Inst. Wash. publication No. 201.

and Hoobler,[16] Fleming,[8] Talbot,[17] Fleming and Hutchison,[4] and others, to be greater than that of the normal infant. It is of interest, however, to consider whether the heat output is greater per kilogram of active metabolic tissue with the marantic infant than with the normal infant, as Benedict and Talbot[18] have shown that the active mass of protoplasmic tissue determines the fundamental metabolism. Fleming concluded as a result of a study of his own figures and those of Benedict and Talbot,[15] that about 35 per cent. of the normal infant is composed of tissue inactive metabolically. In a later article, Talbot[17] places this figure at 20 per cent. but bases his conclusion on a consideration of the heat production per kilogram of actual weight and not on the expected weight. When considered on the basis of the expected weight as shown in Figure 2 of his article, his results bear out Fleming's conclusion.[19] It is evident that this figure of 35 per cent. does not take into account the bones, ligaments and other comparatively inactive metabolic tissues which do not vary with the condition of the infant, but is largely confined to the fat and glycogen reserves which are markedly reduced, if not practically absent in the marantic infant. Therefore, if we are to compare the marantic infant with the normal infant, we must consider the weight of the marantic infant as being 65 per cent. of what it would be if it were a normal infant, and make all calculations on the basis of this additional weight.

Fleming[8] found the average heat output of the normal infant to be 54.2 calories per kilogram per day, while for the marantic infant calculated on the basis of the normal infant, he found an output of 60.1 calories (Chart 5 of his article). However, there is an error in his method of calculation which when corrected makes the heat output per kilogram per day to be 52.2 calories for the marantic infant (calculated from the figures in Table 2 of his article), as compared to the normal of 54.2.[20] A study on the same basis of Talbot's[17] figures shows an average heat output for the markedly marantic infant of 58.5 calories

16. Murlin, J. R., and Hoobler, B. R.: The Energy Metabolism of Ten Hospital Children, Between the Ages of Two Months and One Year, Am. J. Dis. Child. **9**:81 (Feb.) 1915.

17. Talbot, F. B.: Severe Infantile Malnutrition, Am. J. Dis. Child. **22**:358 (Oct.) 1921.

18. Benedict, F. G., and Talbot, F. B.: Studies in the Respiratory Exchange of Infants, Am. J. Dis. Child. **8**:1 (July) 1914.

19. Talbot, in a personal communication (June 1925), states that it would seem reasonable to conclude that most of the patients studied have lost 30 per cent. or more of their expected weight before their active protoplasmic tissue was affected. He considers, however, that if the malnutrition is produced rapidly, the body protein would be involved earlier than if the malnutrition developed slowly.

20. Fleming obtained the calculated weight of his marantic infants by adding on 35 per cent. to their actual weight, instead of taking their actual weight as being 65 per cent. of their calculated weight.

per kilogram per day, which is at the upper limit of the normal range. Also the figures for the markedly marantic infants, reported in Table 9 of the article by Fleming and Hutchison,[4] when considered on this basis give an average value of 52.5 calories per kilogram per day. We may therefore conclude that the heat output per kilogram of active metabolic tissue is approximately the same with the marantic infant as with the normal infant.

It is obvious that the marantic infant has not the insulating layer of fat which the normal infant has. This in itself would tend to an increased heat loss. An evidence of this is an increase in the surface temperature of marantic infants found by McClure and Sauer.[21] The effort of the marantic infant to conserve its heat no doubt accounts for the diminished peripheral blood flow reported by Utheim.[2] There is no evidence, however, to indicate that there is any marked abnormality in the heat production but rather that there may be a slightly increased heat production in response to an increased heat loss. This is apparently the view recently expressed by Fleming and Hutchison,[4] who conclude "that the disturbance of metabolism in marasmus is simply the result of inanition and not the cause."

GENERAL CARBOHYDRATE METABOLISM OF THE MARANTIC INFANT

The figures reported by Mattill, Mayer and Sauer[22] on the sugar metabolism of marantic infants are of considerable interest. These investigators found that 0.9 gm. of glucose per kilogram of body weight per hour could be injected into normal infants without causing sugar to appear in the urine. With marantic infants, however, they were able to inject an average of 1.6 gm. of glucose per kilogram per hour before sugar appeared in the urine. When we calculate what these infants would weigh if they had the normal amount of inactive metabolic tissue and divide the amount of glucose injected by this calculated weight, we find that these infants handled 1.04 gm. of glucose per hour per kilogram of calculated weight. It is evident that, calculated on the basis of the active metabolic tissue, the capacity of these marantic infants to utilize injected glucose is approximately the same as for the normal infant.

Our observations on the ability of the marantic infant to remove injected glucose from the blood stream confirm these findings. We found, as illustrated in Chart 1, that the marantic infant removes injected

21. McClure, W. B., and Sauer, L. W.: The Influence of Clothing on the Surface Temperature of Infants, Am. J. Dis. Child. **10**:425 (Dec.) 1915.

22. Mattill, P. M.; Mayer, K. M., and Sauer, L. W.: Dextrose. Tolerance in Atrophic Infants, Am. J. Dis. Child. **19**:42 (Jan.) 1920.

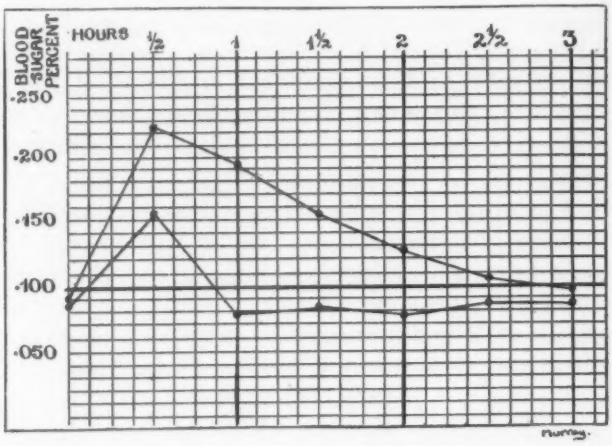

Chart 1.—The lower line represents the average sugar tolerance curve obtained after the subcutaneous injection of 10 c.c. per pound of body weight of a 10 per cent. solution of glucose to marantic infants. The upper line represents the average curve obtained with normal infants.

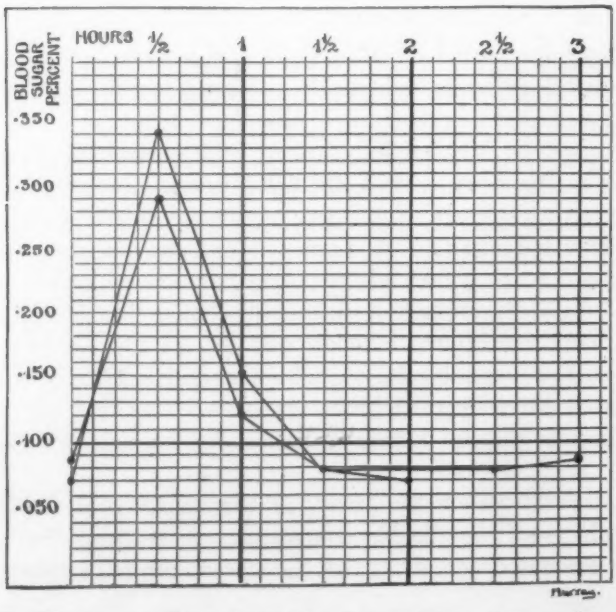

Chart 2.—The upper line represents the average sugar tolerance curve obtained after the intravenous administration of 15 c.c. per pound of body weight of a 10 per cent. solution of glucose to marantic infants. The lower line represents the curve obtained in normal infants after the intravenous administration of 10 c.c. per pound of body weight of the same solution.

glucose from the blood stream more rapidly than the normal infant when the amount given is determined on the basis of the actual weight. However, when the amount given is calculated on the basis of the active metabolic tissue present, we find that the marantic infant removes injected glucose with the same rapidity as the normal infant (Chart 2).

This consideration of the carbohydrate metabolism of marantic infants indicates that there is no derangement in the digestion and absorption of carbohydrate, and that glucose after it reaches the blood stream is removed at approximately the normal rate. The question arises: Is the glucose oxidized and stored in the normal manner? Fleming [4] found the respiratory quotient of marantic infants to be the same as normal infants, which would indicate that there was no very marked derangement of the metabolism of carbohydrate or fat. It is to be remembered, however, that a slight or even moderate derangement of the carbohydrate metabolism might not cause any change in the respiratory quotient. This aspect of the problem is most difficult to investigate. It is obviously impossible to determine directly the amount of glycogen stored by the marantic infant after the injection of glucose. Further studies on the respiratory quotient before and after the injection of glucose, similar to those reported by Sanger and Hun [23] on the adult, might give some information of value.

The only abnormality we have been able to find in the carbohydrate metabolism of marantic infants is that the average fasting blood sugar is about 10 per cent. lower than that of the normal infant. Rumpf [24] found a similar reduction in the blood sugar of infants who had been starved for twenty-four hours. This tends to corroborate the view that the glycogen store of the marantic infant is less than that of the normal infant. We may conclude, therefore, from the evidence available that the marantic infant absorbs and metabolizes carbohydrate in a normal manner, with the exception that it has not the stabilizing influence on the fasting blood sugar level of an adequate reserve of glycogen.

THE CALORIC REQUIREMENTS OF THE MARANTIC INFANT

It is obvious that the caloric requirements for the marantic infant, on the basis of body weight, are greater than for the normal infant. However, if we consider the requirements on the basis of the active protoplasmic mass, and, when comparing the marantic infant with the normal infant, make due allowance for the inactive metabolic tissue which is absent in the marantic infant, we find that if the caloric require-

23. Sanger, B. J., and Hun, E. G.: The Glucose Mobilization Rate in Hyperthyroidism, Arch. Int. Med. **30**:397 (Sept.) 1923.

24. Rumpf, F.: Jahrb. f. Kinderh. **105**:321, 1924.

ments of the normal infant are taken as 45 calories per pound per day, the marantic infant requires $45 \times \frac{100}{65} = 70$ calories per pound per day.

For the last few years we have empirically fed marantic infants from 70 to 100 calories per pound per day. The reason for the beneficial results obtained is at once obvious. A diet of less than 70 calories per pound for the marantic infant amounts to a starvation diet. In view of the possibility of a somewhat increased heat loss from these infants, and the necessity of building up a store of fat and glycogen, it is seen that there is a scientific foundation for feeding these infants from 70 to 100 calories per pound of body weight per day.

CONCLUSIONS

1. There is no evidence from a review of the literature and from our own work that the marantic infant is not able to digest and absorb carbohydrate as readily as the normal infant.

2. The average concentration of the fasting blood sugar of the marantic infant is about 10 per cent. lower than that of the normal infant.

3. From a review of the literature, no evidence is found of any marked abnormality in the heat production of the marantic infant. Any increased heat production, considered on the basis of the mass of active protoplasmic tissue, apparently is in *response* to an increased heat loss, due to a lack of the normal insulating layer of fat.

When feeding the marantic infant, it should be remembered that on the basis of the mass of active protoplasmic tissue, 70 calories per pound per day for the marantic infant is the exact equivalent of 45 calories per pound per day for the normal infant.

4. From a review of the literature and our own work, there is no evidence of any abnormality of the general carbohydrate metabolism of the marantic infant, other than the lowered concentration of fasting blood sugar. This is apparently the result of an inadequate reserve of glycogen.

THE CARBOHYDRATE METABOLISM OF INFANTS WITH DIARRHEA, INFECTIONS AND ACUTE INTESTINAL INTOXICATION

WITH A NOTE ON THE USE OF INSULIN *

FREDERICK F. TISDALL, M.D. (Tor.)
T. G. H. DRAKE, M.B. (Tor.)
AND
ALAN BROWN, M.B. (Tor.)
TORONTO, CANADA

In other papers, we have considered the carbohydrate metabolism of the normal and the marantic infant. In the present paper we will present some studies we have made on the carbohydrate metabolism of infants with diarrhea, infection and intoxication.

THE AVERAGE CONCENTRATION OF THE FASTING BLOOD SUGAR

A review of the literature discloses very conflicting results. Cobliner [1] reported a hyperglycemia in some patients with fever, but found normal values in those with intestinal intoxication. A marked increase in the percentage of blood sugar in infants with diarrhea was found by Bing and Windelow,[2] and also by Gotzky.[3] A tendency to hyperglycemia in infants with alimentary intoxication was observed by Mogwitz.[4] Quite high values were found by Niemann [5] in infants with fever or acute intestinal disturbances. Chapin and Myers,[6] and Brown [7] obtained normal values in infants with diarrhea.

We determined the fasting blood sugar in twenty-eight infants with an elevation of temperature (exclusive of acute intestinal intoxication), of from 2 to 6 degrees. The average value found was 0.089 per cent. In five infants with diarrhea an average value of 0.077 per cent. was

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* From the Wards and Nutritional Research Laboratories of the Hospital for Sick Children, and the Sub-Department of Pediatrics, University of Toronto.

1. Cobliner, S.: Ztschr. f. Kinderh. **1**:207, 1911.
2. Bing, H. J., and Windelow, O.: Ztschr. f. Kinderh. **9**:64, 1913.
3. Gotzky: Ztschr. f. Kinderh. **9**:44, 1913.
4. Mogwitz: Monatschr. f. Kinderh. **12**:569, 1914.
5. Niemann, A.: Jahrb. f. Kinderh. **83**:1, 1916.
6. Chapin, H. D., and Myers, V. C.: Chemical Examination of the Blood in Children, Am. J. Dis. Child. **18**:555 (Dec.) 1919.
7. Brown, M. J.: Quart. J. Med. **18**:175 (Jan.) 1925.

obtained, while in thirteen infants suffering from acute intestinal intoxication the average percentage was 0.102 per cent. The temperature of practically all the infants with acute intestinal intoxication ranged from 100 to 103 F. The reason for the conflicting results found by different investigators in infants with diarrhea, fever or intoxication will be discussed later.

THE SUGAR TOLERANCE CURVES OBTAINED AFTER THE INTRAVENOUS AND SUBCUTANEOUS ADMINISTRATION OF GLUCOSE

Ten cubic centimeters per pound of body weight of a 10 per cent. solution of glucose was administered intravenously to five infants suffering from diarrhea. The diarrhea was of the type ordinarily encountered in the summer months, the stools were loose and numbered from six to ten in twenty-four hours. None of the infants showed any signs of intoxication. In two of the infants the added sugar disappeared from the blood stream with almost the normal rapidity, while in the other three the blood sugar remained at a much higher level. A curve plotted from the average values obtained in these five cases is shown in Chart I. A discussion of these results will be reserved until we have presented our findings in the other abnormal conditions.

Ten cubic centimeters per pound of body weight of a 10 per cent. solution of glucose was given intravenously to twenty-four infants with fever. The temperature ranged from 100 to 106 F., with an average of 101.7 F. The elevation of temperature accompanied the following clinical conditions: rhinopharyngitis, otitis media, bronchitis, bronchopneumonia, pyelitis, eczema, intussusception and postanesthetic acidosis. With the exception of two patients with otitis media and one with bronchitis, in which the elevation of temperature was very slight or of short duration, the glucose was not removed from the blood stream with the normal rapidity. Many of these infants showed no clinical evidences of any toxic effect from the disease. A curve plotted from the average values found in these cases is shown in Chart 2. It is seen that the blood sugar, instead of returning to the original level in from one to one and a half hours as with the normal infant, was still at the abnormal level of 0.183 per cent. at the end of the one and a half hour period.

A number of infants with fever were given subcutaneous injections of 10 per cent. glucose, and the blood sugar was determined at half hourly intervals for three hours. A curve plotted from the average values found in these cases is given in Chart 3. The same delayed reaction is seen to occur with the subcutaneous as with the intravenous administration of glucose.

Ten cubic centimeters per pound of body weight of a 10 per cent. solution of glucose was given intravenously to thirteen infants suffering

from acute intestinal intoxication. All these infants showed signs of a varying degree of intoxication; loose greenish stools with mucus, sunken eyes, drowsiness, frightened appearance when aroused and sometimes an accompanying acidosis as evidenced by hyperpnea. The temperature ranged from 100 to 103 F. A curve plotted from the average blood sugar values found in these cases is shown in Figure 2. It is evident that the same type of reaction is obtained with these infants as with infants with fever due to other causes. With these cases, however, the injected glucose is removed from the blood stream even more slowly than with the preceding group.

THE EFFECT OF THE ADMINISTRATION OF INSULIN

Marriott [8] and others have recommended the use of insulin in the treatment of marantic infants and claim to have obtained very beneficial results. Unfortunately, we have not been able to confirm their observations.[9] As no abnormalities have been found in the carbohydrate metabolism of marantic infants,[10] there is no theoretic indication that insulin would be of benefit in this type of case.

In the present study, we have shown that in infants with fever there is usually a marked delay in the reduction of the blood sugar concentration after the injection of glucose. On this account we gave insulin in conjunction with the intravenous administration of 10 c.c. per pound of body weight of a 10 per cent. solution of glucose to twelve infants with fever. The insulin was usually given subcutaneously half an hour before the glucose. The amount of insulin administered varied from one unit for each 6 gm. of glucose, to 1 unit for each 1.5 gm. of glucose. The sugar tolerance was determined in each case after the administration of glucose alone and after the administration of glucose plus insulin. In all, 110 blood sugar determinations were made. We found that the effect of the insulin varied tremendously in different infants, an observation we had already made with marantic and normal infants. The most interesting observation, however, is that the effect produced by insulin in these infants with fever was much less than that produced by the same dose in normal infants; in fact, in some patients who were quite toxic, large doses of insulin produced no discernible effect at all.

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8. Marriott, W. McK.: The Food Requirements of Malnourished Infants, J. A. M. A. **83**:600 (Aug. 23) 1924.

9. Tisdall, F. F.; Brown, A.; Drake, T. G. H., and Cody, M. G.: Insulin in the Treatment of Malnourished Infants, Am. J. Dis. Child. **30**:10 (July) 1925.

10. Tisdall, F. F.; Drake, T. G. H., and Brown, A.: The Carbohydrate Metabolism of the Marantic Infant, Am. J. Dis. Child. **30**:329 (Dec.) 1925.

COMMENT

It is well known that in adults a diabetic type of curve is encountered in various diseases other than diabetes. O'Hare [11] has shown that there is a delay in the fall of the sugar tolerance curve in patients with vascular hypertension. In adults with gastro-intestinal cancer, a decrease in the sugar tolerance has been reported by Friedenwald and Grove.[12] It has been found by Pemberton and Foster [13] and confirmed by Fletcher [14] that in cases of chronic arthritis the rise in blood sugar, after the ingestion of glucose, is both increased and prolonged, as compared with the

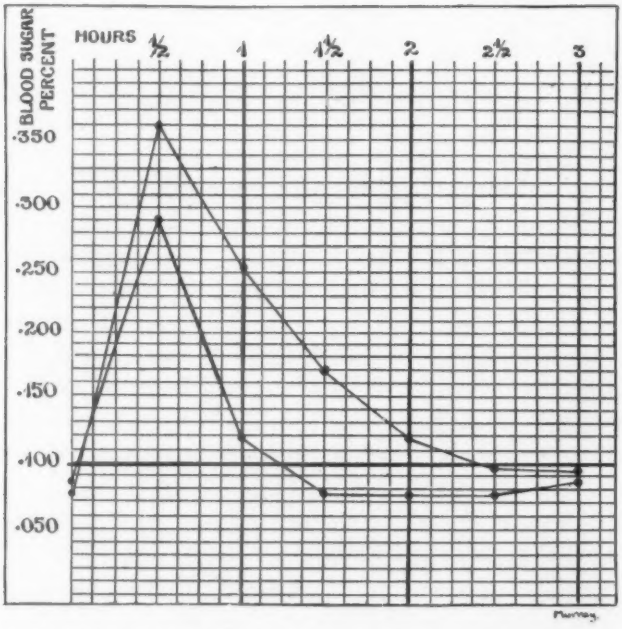

Chart 1.—The upper line represents the average sugar tolerance curve obtained after the intravenous administration of 10 c.c. per pound of body weight of a 10 per cent. solution of glucose to infants with diarrhea. The lower line is the average curve obtained with normal infants.

normal curve. It is recognized clinically that the various glands of internal secretion have a definite effect on the carbohydrate tolerance.

The close association of infection and glycosuria has been known for years, as, for example, the frequent occurrence of glycosuria in

11. O'Hare, J. P.: Am. J. M. Sc. **160**:366 (Sept.) 1920.

12. Friedenwald, J., and Grove, G. H.: Am. J. M. Sc. **160**:313 (Sept.) 1920.

13. Pemberton, R., and Foster, G. L.: Studies on the Nitrogen, Urea, Carbon Dioxid Combining Power, Calcium, Total Fat and Cholesterol of the Fasting Blood, Renal Function, Blood Sugar and Sugar Tolerance, Arch. Int. Med. **25**: 243 (March) 1920.

14. Fletcher, A. A.: Dietetic Treatment of Chronic Arthritis and Its Relationship to the Sugar Tolerance, Arch. Int. Med. **30**:106 (July) 1922.

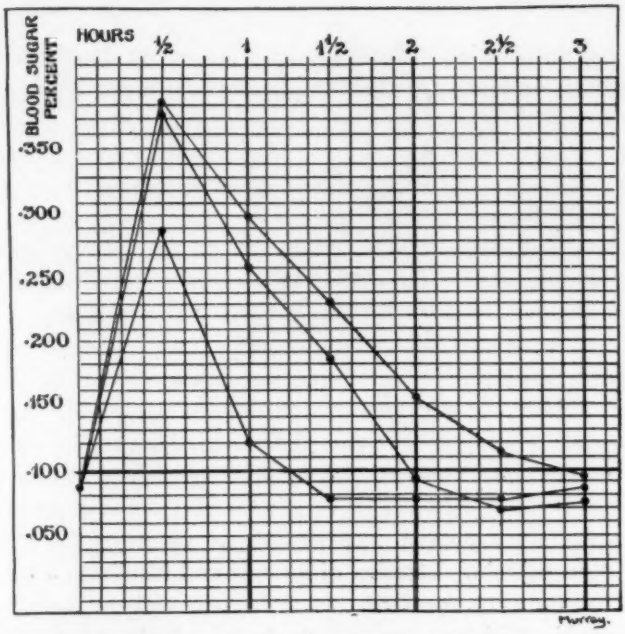

Chart 2.—The upper line represents the average sugar tolerance curve obtained after the intravenous administration of 10 c.c. per pound of body weight of a 10 per cent. solution of glucose to infants with acute intestinal intoxication. The middle line is the average curve obtained with infants with infection and the lower line the curve obtained with normal infants.

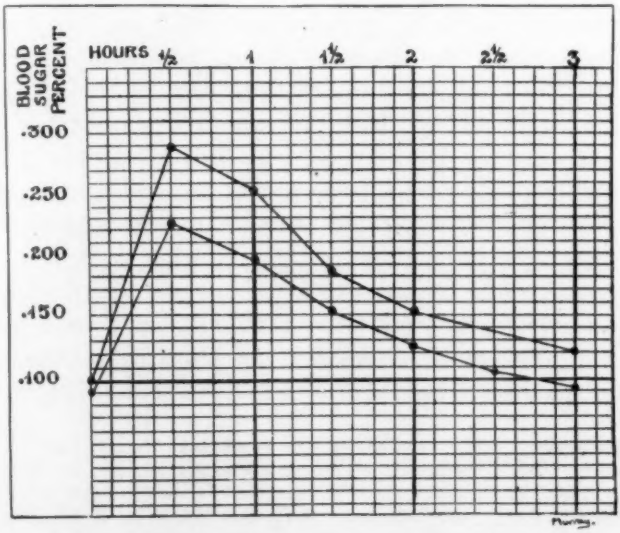

Chart 3.—The upper line represents the average sugar tolerance curve obtained after the subcutaneous administration of 10 c.c. per pound of body weight of a 10 per cent. solution of glucose to infants with infection. The lower line is the average curve obtained with normal infants.

patients suffering from carbuncles. So far as we have been able to find, however, no sugar tolerance curves have been previously published to show the effect of infection of the blood sugar level. Examination of Figures 1, 2 and 3 shows that there is a definite reduction in the ability of infants with diarrhea, fever or intoxication to remove injected glucose from the blood stream.

The fact that these infants are unable to remove injected glucose from the blood stream at the normal rate would seem to indicate the use of insulin in the treatment of these cases. This inability to remove injected glucose at the normal rate, however, might be due to factors other than a deficient supply of insulin. With adults, Rabinowitch,[15] Banting, Campbell and Fletcher,[16] Campbell and MacLeod,[17] and others, have found that the action of insulin is definitely lessened by the presence of an infection. We observed the same phenomena with infants. To test out any possible benefit that might result from the use of insulin to infants with infections or intoxication, we observed the effects produced by repeated administration of glucose and insulin to a large series of cases. The results obtained, however, were quite disappointing, as we were unable to detect any definite beneficial effect.

It might be construed that the lessened ability of these infants to remove injected glucose from the blood stream might be an indication for the reduction of carbohydrate. This, both on theoretic and clinical grounds, is not the case. It has been shown by Foster,[18] Traugott,[19] and others, that the administration of carbohydrate stimulated the ability of the organism to metabolize carbohydrate, and it was found by Beck [20] that fasting lowered the tolerance for carbohydrate. Clinically, we obtained the best results in many of these cases by the administration of glucose. In infants who have died with toxemia, there is usually a large amount of fat in the liver and very little glycogen. It is known that the presence of glycogen helps protect the organisms against toxemia, and so we have a definite rationale for the administration of carbohydrate.

Our results would indicate that in infants with diarrhea, fever due to various infections, or acute intestinal intoxication, there is a derangement of the carbohydrate metabolism not primarily associated with a deficient production of insulin.

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15. Rabinowitch, I. M.: Canad. M. A. J. **14**:481 (June) 1924.
16. Banting, F. G.; Campbell, W. R., and Fletcher, A. A.: J. Metabol. Res. **2**:547 (Nov.-Dec.) 1922.
17. Campbell, W. R., and MacLeod, J. J. R.: Medicine **3**:195 (Aug.) 1924.
18. Foster, G. L.: J. Biol. Chem. **55**:303 (Feb.) 1923.
19. Traugott, C.: Klin. Wchnschr. **1**:2384, 1922.
20. Beck, W.: Ztschr. f. klin. Med. **98**:465 (March) 1924.

SUMMARY

Glucose injected into the blood stream of infants with diarrhea, infection or acute intestinal intoxication is not removed as rapidly as in the normal infant.

Our results would indicate that in infants with diarrhea, infection or acute intestinal intoxication, there is a derangement of the carbohydrate metabolism not primarily associated with a deficient production of insulin.

THE COLLOIDAL BENZOIN REACTION

IN ACUTE POLIOMYELITIS *

JOSEPH C. REGAN, M.D.
BROOKLYN

Guillain, Laroche and Lechelle [1] have published the description of a new test of the cerebrospinal fluid called the colloidal benzoin reaction, which they have found of more precise value in the diagnosis and prognosis of syphilitic disease of the central nervous system than either the gold chlorid or the mastic test.

This colloidal reaction has, according to the originators of the method, several obvious advantages over the gold chlorid test. Thus, the reading of the results are more simple, as it is a question of a precipitation and not of a color change. Then again the suspension of benzoin is very simple to prepare, avoiding the technical difficulties so often encountered in the preparation of a reliable colloidal gold solution. Finally, a fact of great importance, is that reactions occurring in Tubes 1 to 5 are strictly limited to syphilitic disease of the central nervous system (with the exception of certain cases of tuberculous meningitis).

TECHNIC OF THE COLLOIDAL BENZOIN REACTION

Glassware: The glassware required is composed of sixteen tubes (1 cm. by 6 cm.), suitable pipets and flasks which must be of nonsoluble glass. Before use, this glassware is prepared by washing first in an aqueous solution of hydrochloric acid (2 per cent.) and then twice in distilled water.

Solutions Used: Two solutions are employed, namely, a saline solution containing 0.1 gm. of chemically pure sodium chlorid to 1,000 c.c. of twice distilled water, and a homogeneous suspension of the resin of benzoin in distilled water prepared as follows:

Dissolve 1 gm. of the natural resin of benzoin (Sumatra) in 10 c.c. of absolute alcohol for forty-eight hours. The limpid liquid obtained is poured off and preserved as a stock alcoholic solution. When a reaction is to be performed, 0.3 c.c. of this alcoholic solution is added slowly to 20 c.c. of twice distilled water heated to 35 C. in such a manner as

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* From the Kingston Avenue Hospital of the Bureau of Hospitals, Department of Health, New York City, Dr. Frank J. Monaghan, Commissioner, S. B. Wynne, Director, and Dr. Donald D. Campbell, Physician in Charge.

1. Guillain, G.; Laroche, G., and Lechelle, P.: La reaction du benzoin colloidal avec le liquide cephalo-rachidien dans l'encéphalitie lethargique, Rev. Neurol., January, 1921, p. 80.

to obtain a very homogeneous suspension. This suspension of benzoin must be freshly prepared and must not be kept more than a few days. The water used must be recently distilled.

THE ACTUAL TECHNIC OF THE REACTION

(*A*) With a suitable pipet, add to the various tubes mentioned the following quantity of sodium chlorid solution (0.1 gm. per thousand cubic centimeters).

To tube 1, 0.25 c.c. of sodium solution.
To tube 2, 0.50 c.c. of sodium solution.
To tube 3, 1.50 c.c. of sodium solution.
Tubes 4 to 16 inclusive, 1 c.c. of the same saline solution.

(*B*) Then pipet, shaking the mixture carefully after adding it to each tube the following amounts of cerebrospinal fluid.

To tube 1, 0.75 c.c. of cerebrospinal fluid.
To tube 2, 0.50 c.c. of cerebrospinal fluid.
To tube 3, 0.50 c.c. of cerebrospinal fluid.

(*C*) Then take 1 c.c. of the contents of Tube 3 and carry it over with a pipet to Tube 4. Mix the contents of Tube 4 well by aspirating with a pipet several times and carry over 1 c.c. of the mixture to Tube 5. Continued this until Tube 15 is reached, and reject 1 c.c. of this tube without putting it into Tube 16, which serves as a control.

(*D*) Into each tube add 1 c.c. of the benzoin suspension. The contents of all the tubes will then be of a milky homogeneous aspect.

(*E*) The dilutions of the cerebrospinal fluid will then vary in geometric progression from ½ in Tube 2 up to $\frac{1}{16,384}$ in Tube 15. The reaction is read in from six to twelve hours.

INTERPRETATION

(*A*) In the negative tubes the aspect of uniform homogeneous turbidity persists without precipitation. These tubes are similar to the control. Such a reaction is designated numerically as a 0.

(*B*) In the positive tubes the precipitation of benzoin is absolute, the liquid is completely clarified and has the aspect of clear water, and the benzoin is completely sedimented at the bottom of the tubes. The complete reaction is designated numerically as 2.

(*C*) Between the two varieties there exists a subpositive reaction. The tube retains then a varying modification of the turbidity but does present a more or less abundant sediment. This is designated then numerically as 1.

TABLE 1.—*Colloidal Benzoin Reaction in Acute Poliomyelitis. Table of Spinal Fluids with Summary of Cases*

Case	Date of Onset	Type of the Disease	Paralysis	Day of Disease Spinal Fluid Obtained	Colloidal Benzoin Reaction	Cell Count	Quantitative Albumin, Globulin	Albumin	Gm. per Liter	Fehlings	Termination
1	8/17/23	Ascending Landry's...	Lowers, back, respir., deglut.....	2d	000001221000000	90	1+	1+	0.40	3+	Died
2	8/27/23	Myelitic bulbopontine.	Rt. upper, palate, tongue, pharynx, face, palate	4th	000002221000000	22	—	—	0.22	3+	Recovered
3	8/17/23	Myelitic.....	Weakness lower extremities.....	8th	000002221000000	..	—	—	0.22	3+	Recovered
4	8/16/23	Myelitic bulbopontine.	Both lowers, bilat. ophthalmoplegia, face, diaphragm, both uppers	9th	000000212221000	62	1+	3+	1.4	3+	Recovered
				14th	000002211000000	40	—	—	0.22	3+	
				46th	000000100000000	..	—	—	....	3+	
5	8/ 2/23	Myelitic.....	Rt. lower and lt. upper.....	11th	000001222210000	40	1+	2+	0.85	3+	Recovered
				20th	000000212220000	15	1+	2+	0.85	3+	
6	8/ 9/23	Myelitic.....	Rt. upper and rt. lower.....	12th	000002222100000	—	1+	1+	0.40	3+	Recovered
				13th	000002222100000	5	1+	1+	0.40	3+	
				18th	000002222100000	5	1+	1+	0.40	3+	
7	8/10/23	Myelitic (rudiment)....	Lt. foot (weak).....	12th	000002222100000	10	—	—	0.22	3+	Recovered
				13th	000002221000000	5	—	—	0.22	3+	
				17th	000002222100000	5	—	—	....	3+	
8	7/23/23	Myelitic bulbar.....	Upper extrem., palate and face...	16th	000000222120000	5	1+	1+	0.56	3+	Recovered
9	8/13/23	Myelitis bulbar pontine	Weakness, lower extrem., ptosis...	17th*	001111022221000	..	...	...	....	...	Recovered
				30th	000000222000000	..	...	...	....	...	
10	7/25/23	Myelitic.....	Both lower extrem., neck, back...	19th	000001222100000	15	1+	—	....	3+	Recovered
				24th	000000122100000	..	1+	1+	0.40	3+	
				30th	000001222200000	7	1+	1+	....	3+	
				36th*	001022221000000	5	...	...	0.22	3+	
11	7/25/23	Myelitic.....	Both lowers, neck and back.....	21st	000001022200000	..	...	...	....	...	Recovered
12	7/29/23	Myelitic.....	Rt. lower extrem.....	22d	000000222100000	5	1+	2+	0.76	3+	Recovered
				27th	000002112200000	0	1+	2+	0.76	3+	
				32d	000002222210000	..	...	...	....	...	
13	7/19/23	Bulbopontine.....	Face, pharynx, palate.....	25th	000001222200000	40	1+	—	....	3+	Recovered
14	7/16/23	Myelitic.....	Both lower extremities.....	23d	000002222000000	15	1+	1+	0.40	3+	Recovered
				27th	000001222100000	15	1+	1+	....	3+	
15	7/14/23	Myelitic.....	Left lower extremity.....	30th*	000122222211000	100	2+	2+	0.85	3+	Recovered
16	7/13/23	Myelitic.....	Both lower extremities.....	32d	000000222111000	0	1+	—	....	3+	Recovered
17	7/14/23	Myelitic.....	Left lower extremity.....	34th	000002221100000	10	—	—	0.22	3+	Recovered
18	7/ 1/23	Myelitic bulbar.....	Left arm, leg, back, neck, respir., muscles weak	45th	000002220000000	3	—	—	0.22	3+	Recovered
19	6/28/23	Myelitic.....	Weakness, both lowers.....	48th	000000110000000	20	—	—	0.22	3+	Recovered
20	7/29/23	Myelitic.....	Right lower extremity.....	43d	000000222100000	10	1+	2+	0.56	3+	Recovered
				50th	000000222100000	5	1+	2+	0.56	3+	
21	7/27/23	Myelitic pontine.....	Right lower weak, right int. strabismus	6th	000002211000000	40	—	—	0.22	3+	Recovered
				25th	000001221000000	..	—	—	....	3+	
				30th	000002220000000	40	—	—	0.22	3+	
				39th	000000110000000	2	—	—	0.22	3+	
22	8/ 9/23	Myelitic.....	Right upper and lower.....	26th	000002222000000	7	—	1+	0.40	3+	Recovered
				37th	000000000000000	0	—	—	0.22	3+	
				46th	000000000000000	0	...	...	....	...	
23	8/20/23	Myelitic.....	Both lower extremities weak.....	21st	000000222000000	..	—	—	....	3+	Recovered
				22d	000000000000000	..	—	—	0.22	3+	
				34th	000000000000000	17	...	...	....	3+	
				41st	000000222000000	35	—	—	....	3+	
				50th	000000000000000	17	—	—	....	3+	
24	9/22/23	Myelitic.....	Both lower extremities, right upper weak	23d	000000221000000	5	1+	1+	0.56	3+	Recovered
				26th	002000221000000	2	1+	1	0.40	3+	
				68th	000000000000000	5	—	1+	0.37	3+	

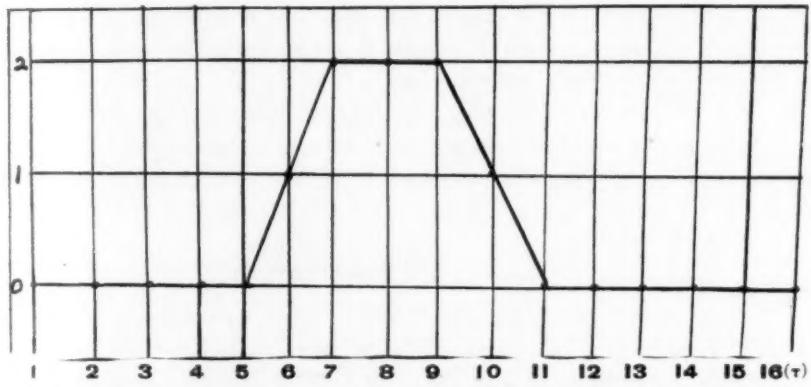
* Fluids slightly blood stained.

(*D*) A normal cerebrospinal fluid, according to the originators of the method, may give some precipitation in Tubes 6 and 7.

(*E*) Two zones of reaction have been described, one a reaction in the syphilitic zone, Tubes 1 to 5, the other a reaction in the meningitic zone, Tubes 6 to 15.

TYPES OF REACTIONS ENCOUNTERED IN CERTAIN ACUTE INFECTIONS OF THE CENTRAL NERVOUS SYSTEM

Space will not permit the description in detail of the various types of curves encountered in syphilis of the central nervous system, but it may be said briefly that the first five tubes are always partly or completely concerned. It is especially, however, in relation to the reactions encountered in the meningitic zone in certain of the acute infectious



An average curve in acute poliomyelitis. Reading: 000002221000000.

diseases of the central nervous system that I wish to discuss the test at this time. To do so it will be necessary to refer briefly to certain observations already made by various authors.

Guillain and Lechelle [1] have reported nine cases of epidemic encephalitis in which the colloidal benzoin reaction was negative. Duhot and Crampton [2] have reported negative results in six cases of the same disease. Bregi [3] has observed thirteen and Rabeau [4] ten, in all of which this colloidal test was normal.

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2. Duhot, E., and Crampton, P.: Encéphalite epidemique et reaction de Bordet Wassermann, Bull. et mém. Soc. méd. d. hôp. de Paris **45**:587 (April 21) 1921.

3. Bregi, L.: L'étude sur lar reaction du benzoin colloidal dans le liquide cephalo-rachidien, Thésè de Lille, 1921.

4. Rabeau, H.: Valeur comparee de la reaction du benzoin colloidal, Compt. rend Soc. de biol. **85**:704 (Oct. 22) 1921.

* Fluids slightly blood stained.

On the other hand, Guillain, Laroche and Lechelle [5] have observed in eleven cases of tuberculous meningitis a positive reaction in what they term the meningitic zone, the precipitation starting in Tubes 6 or 7 and being prolonged more or less far, sometimes to Tubes 13, 14 or 15, at others only to Tube 12. Occasionally, there was observed a slightly different type of precipitation, in that there were two phases in the curve, a rise in the syphilitic zone (Tubes 1 to 5), then a fall to normal and subsequent elevation in the meningitic zone, Tubes 6 to 12 or 14.

The observation, that the cerebrospinal fluid in epidemic encephalitis does not react with colloidal benzoin, may be of further practical value in assisting the differentiation of that disease from the various forms of cerebrospinal syphilis which may resemble it clinically. This is more especially the case because the Wassermann reaction is not apparently absolutely reliable in this regard, for it has been shown to be positive in some exceptional cases of epidemic encephalitis without any evidence of syphilis of the nervous system being present (Achard and Leblanc,[6] Raymond,[7] Duhot and Crampton [2]).

So far as I could determine, no reference has yet been made to the character of the colloidal benzoin reaction in acute poliomyelitis. It was considered desirable to study a series of fluids from the latter disease to find out the type of precipitation, if any, which might occur.

DETAILS OF PRESENT STUDY

During the summer and fall of 1923, a small outbreak of acute poliomyelitis occurred in Brooklyn. The colloidal benzoin reaction was performed as a routine test on the spinal fluids of twenty-three of the patients who were admitted to the hospital.

A total of fifty spinal fluids from these twenty-three patients were examined. The fluids were taken at various intervals from the fourth to the sixty-eighth day of the disease.

Divided in accordance with the weeks in which they were obtained, the fluids were distributed as follows:

First week, 3 fluids; second week, 7 fluids; third week, 9 fluids; fourth week, 12 fluids; fifth week, 7 fluids; sixth week, 4 fluids; seventh week, 5 fluids; eighth week, 2 fluids; tenth week, 1 fluid.

5. Guillain, G.; Laroche, G., and Lechelle, P.: La reaction de benzoin colloidal dans la meningite tuberculeuse, Compt. rend. Soc. de biol. **84**:81 (Jan. 15) 1921.

6. Achard, C., and Leblanc, A.: Encéphalite epidemique, forms prolongee, troubles de l'equilibre, Bull. et mem. Soc. méd. d. hôp. de Paris **44**:668 (May 14) 1920.

7. Raymond, L.: Discussion a l'occasion de la communication de Achard and Leblanc, footnote 6, p. 674.

RESULTS OBTAINED

A reaction was encountered in every spinal fluid examined during the first three weeks of the disease, except in one instance.

ZONE IN WHICH REACTION OCCURRED

The precipitation was encountered with fair constancy in the lower dilutions of the meningitic zone, namely, in Tubes 6, 7, 8, 9 and often involving 10. Occasionally Tube 11 and rarely Tube 12 showed a precipitation. Thus, out of fifty fluids, in only six did the reaction extend to Tube 11 and in only one to Tube 12.

Occasionally the precipitation did not start until the seventh tube instead of the sixth; this was observed in eight fluids. Less often still was there any reaction observed in the first five tubes. This occurred in but five fluids, and when at all definite seemed to be attributable to the presence of blood. Thus, in two cases in which it was pronounced, the fluids were distinctly blood stained; in two of the three remaining fluids, the precipitation started only with the fifth tube and in the remaining instance it was limited to the third tube.

TABLE 2.—*Total of Fluids*

	Total Number Fluids	Number Fluids Normal
First week	3	0
Second week	7	0
Third week	9	1
Fourth week	12	3
Fifth week	7	2
Sixth week	4	3
Seventh week	5	4
Eighth week	2	1
Tenth week	1	1

DURATION OF THE POSITIVE REACTION

The reaction remained uniformly positive in the first three weeks in the nineteen fluids examined at this time except in one instance (a fluid on the third week of the disease); then the normal reaction began to occur with increasing frequency. Thus, in the fourth week, three of twelve fluids showed normal reactions; in the sixth week, three of four fluids were normal. This is shown in Table 2.

RELATION OF POSITIVE COLLOIDAL BENZOIN TO THE CYTOLOGY AND CHEMISTRY OF THE SPINAL FLUID

There was no relation between the degree of cytologic increase in the spinal fluid and the extent of the precipitation of colloidal benzoin.

There was a rough but definite relationship between the extent of the precipitation of colloidal benzoin and the quantity of albumin and globulin in the spinal fluid. The more widespread the precipitation the

higher as a rule was the globulin and quantitative estimation of albumin in the spinal fluid.

With the decline in the cell count and the slower return to normal of the albumin and globulin content of the spinal fluid, the degree of colloidal benzoin precipitation also diminished following the latter much more closely than the former, however, and often remaining elevated when all other pathologic signs in the spinal fluid had disappeared (except probably the colloidal gold reaction,[8] although this was not ascertained in this study).

SUMMARY

1. A study of the spinal fluid in acute poliomyelitis was made with the colloidal benzoin reaction. A total of fifty fluids from twenty-three patients were examined at intervals varying from the fourth to the sixtieth day of the disease.

2. A reaction was obtained in every spinal fluid examined during the first three weeks of the disease, except in one instance.

3. The precipitation was encountered with fair constancy in the lower dilutions of the meningitic zone, namely, in Tubes 6, 7, 8, 9 and often 10. Occasionally Tube 11 and rarely Tube 12 showed precipitation.

4. In a small number of fluids (eight) the reaction did not start until Tube 7. In a few instances a precipitation occurred in the first five tubes, but when definite and occurring in more than Tube 5 it was attributable to the presence of blood in the fluid.

5. The reaction was almost constantly present in the first three weeks of the disease. From the fourth week on, a negative test occurred with increasing frequency and most fluids examined after the sixth week were normal.

6. There was no relation between the height of the cell count and the extent of the precipitation of colloidal benzoin.

7. There was a rough but definite relation between the quantity of albumin and globulin in the spinal fluid and the extent of the precipitation of colloidal benzoin.

8. The extent of the colloidal benzoin precipitation diminished with the decline in the cell count and albumin globulin content of the spinal fluid, following the latter much more closely than the former, however.

CONCLUSIONS

The fact that the spinal fluid of acute poliomyelitis and tuberculous meningitis appears to give a reaction with colloidal benzoin in the meningitic zone, with fair constancy, offers an additional and probably valuable means of differentiating these diseases from epidemic encephalitis.

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8. Regan, J. C.; Litvak, A., and Regan, C.: The Colloidal Gold Reaction in Acute Poliomyelitis, Am. J. Dis. Child. **25**:76 (Jan.) 1923.

DEVELOPMENT AND SIZE OF THE HEART IN CHILDREN

AS REVEALED BY TELEROENTGEN-RAY MEASUREMENTS *

THOMAS ZISKIN, M.D.
MINNEAPOLIS

The importance of the roentgen ray in the examination of patients with cardiac diseases has been definitely established. It gives us valuable information as to the size, shape and position of the heart, also as to the condition of the heart muscle. In adults, the use of the roentgen ray in substantiating cardiac diagnosis has become routine. In children, however, it is only recently that interest has been aroused in the use of the roentgenogram in the diagnosis of heart conditions.

The present investigation was undertaken for the purpose of studying the normal measurements of children's hearts and their relationship to body growth.

Teleroentgenograms were taken at a distance of 6 feet with the patient in the vertical position. Very little difficulty was experienced in getting the cooperation of the children while taking the plates. The phase of respiration was considered a negligible factor, as most observers believe that there is little variance in the size of the heart during inspiration and expiration. Tyson and Borzell [1] state that from their observations, respiratory movements cause very little change in the maximum transverse diameter of the child's heart. Cohn,[2] in a study of the heart measurements in adults, states that in normal breathing the difference in the size of the heart during inspiration and expiration may be ignored.

MEASUREMENTS

The cases were classified both according to height and age and the following measurements were made from the roentgenograms:

1. M. R., distance from the midline to the most distant right border.
2. M. L., distance from the midline to the most distant left border.
3. T. D., the sum of the M. L. and M. R. was taken as the transverse diameter.
4. L. D., the maximum long diameter measured from the auricular notch to the most distant apical border.

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* Received for publication, July 24, 1925.

1. Tyson, R. M., and Borzell, F. F.: Preliminary Observations of Cardiac Measurements in Children, Am. J. Roentgenol. **10**:559 (July) 1923.
2. Cohn, Alfred E.: An Investigation of the Size of the Heart in Soldiers by the Teleroentgen Method, Arch. Int. Med. **25**:499 (May) 1920.

5. B. D., the maximum broad diameter measured at right angles from the long diameter to the most distant borders above and below.

6. Diameter of the aortic arch.

7. The angles formed by the transverse and long diameters.

8. I. D., the maximum internal diameter of the chest.

9. The ratio of the transverse diameter to the internal chest diameter.

10. The ratio of the median right diameter to the median left diameter.

TABLE 1.—*Average Measurements of Diameters and Angle of Heart, Also Ratio of Median Right to Median Left Diameters According to Age. A Variation of 10 Per Cent. Above or Below These Figures May Be Allowed as the Minimum and Maximum of the Normal*

Age	No. of Cases	T. D., Cm.	M. R., Cm.	M. L., Cm.	I. D., Cm.	L. D., Cm.	B. D., Cm.	Aorta, Cm.	Angle, Degrees	M. R. M. L. per Cent.
4	12	8.71	2.90	5.81	18.34	9.64	6.95	3.17	45.7	49.9
5	17	8.51	2.96	5.55	18.77	9.58	7.11	3.38	47.7	53.3
6	39	8.64	3.02	5.62	19.63	9.94	7.29	3.36	48.4	53.7
7	20	9.05	3.02	6.03	20.05	10.26	7.58	3.36	48.2	50.0
8	80	8.91	3.06	5.85	20.46	10.13	7.59	3.48	49.1	52.3
9	49	9.25	3.15	6.10	21.26	10.64	7.74	3.55	49.4	51.6
10	48	9.38	3.15	6.23	21.57	10.93	8.31	3.66	48.0	50.5
11	57	9.59	3.28	6.31	21.77	11.26	7.91	3.57	50.9	51.9
12	20	9.85	3.25	6.60	21.76	11.51	8.58	3.77	49.9	49.2
13	28	9.88	3.37	6.51	23.41	11.76	8.62	3.86	51.0	51.7
14	24	10.38	3.57	6.81	24.44	12.15	9.11	3.94	48.5	52.4
15	26	10.24	3.44	6.80	25.06	12.47	8.81	3.85	52.2	50.5
16	10	10.40	3.54	6.86	25.99	12.58	9.33	3.95	52.5	51.6

TABLE 2.—*Average Measurements of Diameters and Angle of Heart, Also Ratio of Transverse Diameter to Internal Chest Diameter and Median Right to Median Left Diameter, Grouped According to Height. A Variation of 10 Per Cent. Above or Below These Figures May Be Allowed as the Minimum and Maximum of the Normal*

Height Range, Inches	No. of Cases	T. D., Cm.	M. R., Cm.	M. L., Cm.	I. D., Cm.	L. D., Cm.	B. D., Cm.	Aorta, Cm.	Angle, Degrees	Ratio, %	M. R. M. L. %
38-41	14	8.37	2.84	5.53	18.1	9.37	6.80	3.20	46.5	46.37	51.3
41-44	35	8.52	2.82	5.70	18.9	9.56	7.05	3.31	46.5	44.97	49.5
44-47	56	8.58	3.04	5.54	19.7	9.97	7.39	3.42	44.4	44.25	54.8
47-50	77	9.10	3.14	5.96	20.8	10.38	7.71	3.50	48.7	43.66	52.6
50-53	80	9.38	3.14	6.24	21.5	10.82	8.01	3.57	49.4	43.35	50.3
53-56	59	9.58	3.21	6.37	22.1	11.20	8.35	3.62	50.4	43.75	50.3
56-59	43	9.70	3.30	6.40	22.8	11.61	8.49	3.75	51.5	41.68	51.5
59-62	30	10.00	3.29	6.71	24.2	12.04	8.70	3.86	51.4	41.24	49.0
62-65	17	10.50	3.59	6.91	24.7	12.08	9.04	3.97	50.1	42.83	51.9
65-68	14	10.70	3.59	7.11	26.4	13.20	9.39	4.10	51.6	40.70	50.4

The shape of the heart varies greatly in children, some being of the broad, low lying type, while others are of the long and narrow type. Between these extremes all gradations may be found. The measurements, therefore, vary greatly at all ages. The minimum and maximum as well as the average is given for each measurement. From a study of

the charts and tables, it will be seen that there is a definite development of the heart in all measurements, and that this development corresponds with the normal growth of the rest of the body. The figures given may be taken as the normal limits for each age group and each height group. The value of these figures in differentiating the normal from abnormal hearts in children at different ages can readily be seen. The ratio of the transverse diameter to the internal chest diameter varies from 46.3 per cent. in the group ranging in height from 38 to 41 inches, to 40.7 per cent. in the group ranging in height from 65 to 68 inches, showing that the relative proportion of the heart to the chest cavity decreases slightly with the growth of the child.

HEART ANGLE

The angle of the heart varies from an average of 46 degrees in the youngest and smallest group to an average of 52 degrees in the oldest and largest group. It will be seen, therefore, that the heart in early

TABLE 3.—*Ratio Between Median Right and Median Left Diameters at Various Ages*

	Age												
	4	5	6	7	8	9	10	11	12	13	14	15	16
Percentage ratio	49.9	53.3	53.7	50.0	52.3	51.6	50.5	51.9	49.2	51.7	52.4	50.5	51.6

TABLE 4.—*Ratio Between Median Right and Median Left Diameters at Various Height Ranges*

	Height Range in Inches									
	38 to 41	41 to 44	44 to 47	47 to 50	50 to 53	53 to 56	56 to 59	59 to 62	62 to 65	65 to 68
Percentage ratio.....	51.3	49.5	54.8	52.6	50.3	50.3	51.5	49.0	51.9	50.4

childhood tends to assume a broad horizontal position in the chest cavity, and as development and growth of the child take place, the angle of inclination becomes broader and the heart tends to assume more of a vertical position in the chest cavity. This, in a measure, affects also the relative ratio of the transverse diameter of the heart to the internal chest diameter, for as the angle of inclination of the heart increases, the transverse diameter becomes relatively smaller and the relative ratio between the transverse diameter and the internal chest diameter diminishes also.

Tables 3 and 4 show that the ratio of the median right diameter of the heart to the median left diameter is practically constant during the entire period of childhood, and is approximately 50 per cent. at all ages and all height ranges. This would tend to disprove the prevailing opinion that the right border of the heart extends relatively further to

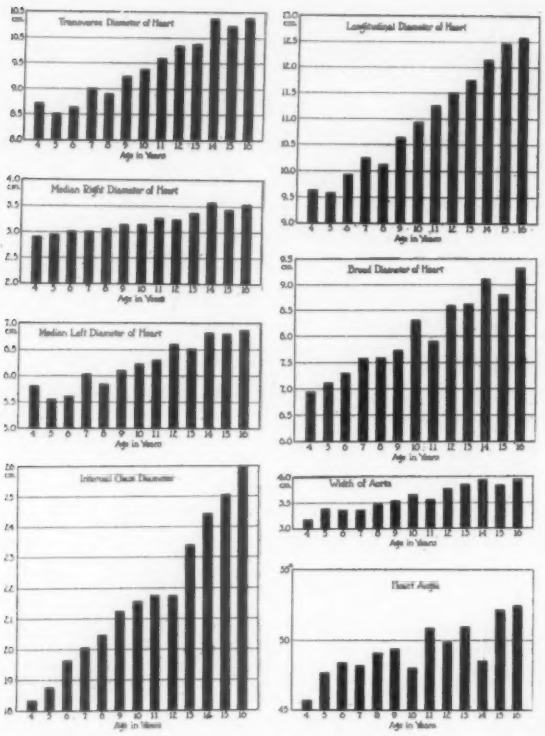


Fig. 1.—Average measurement of diameters and angle of heart grouped according to age.

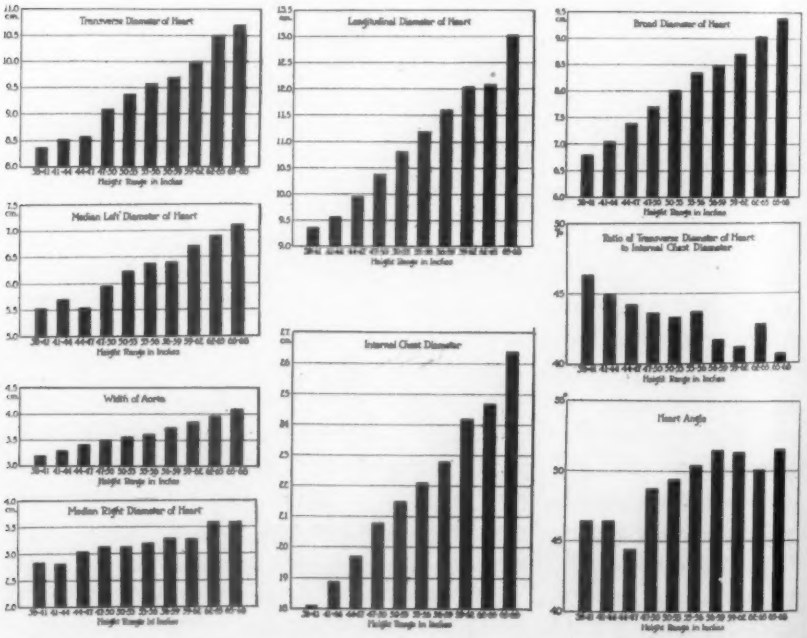

Transverse Diameter of Heart
Longitudinal Diameter of Heart
Broad Diameter of Heart
Median Left Diameter of Heart
Ratio of Transverse Diameter of Heart to Internal Chest Diameter
Internal Chest Diameter
Width of Aorta
Heart Angle
Median Right Diameter of Heart
Height Range in Inches

Fig. 2.—Average measurements of diameters and angle of heart, also ratio of transverse diameter to internal chest diameter grouped according to height.

the right in childhood. We have noted that the ratio between the transverse diameter of the heart and the internal chest diameter tends to diminish during the period of child growth, and the angle of inclination tends to increase during this period, while the ratio between the median right and median left diameters remains practically constant. It may be assumed, therefore, that the decrease in the ratio of the transverse diameter to the internal chest diameter noted in the development and growth of the child, is due entirely to the fact that the angle of inclination of the heart changes from an average of 46 degrees in the smallest and youngest group to an average of 52 degrees in the largest and oldest group.

SUMMARY AND CONCLUSIONS

1. A study was made of the hearts of children by means of the teleroentgenogram.

2. Tables and charts are given, showing the development and relative measurements of the heart at different ages and different heights.

3. The ratio between the transverse diameter of the heart and the internal chest diameter diminishes slightly as the child develops. This is due to the change in the position of the heart.

4. The right border of the heart does not extend relatively further to the right in childhood.

5. There is a constant ratio between the median right diameter and the median left diameter of the heart. This is approximately 50 per cent. at all ages and all heights.

POSTVACCINAL PURPURA

REPORT OF A CASE *

A. B. SCHWARTZ, M.D.
Attending Physician, Milwaukee Children's Hospital
MILWAUKEE

The occurrence of skin rashes following vaccination is frequently noted. In the early days of vaccination, many of these rashes were apparently due to mixed infection incident to vaccine either improperly prepared or administered. With perfected methods of vaccine production and inoculation, such complications or sequellae are infrequent. Within the last few months, practically the entire population of Milwaukee, a city of 500,000, has undergone vaccination. Dr. Koehler,[1] director of health, states that untoward results were practically unobserved.

Eruptions due to the vaccine itself, perhaps more accurately speaking due to the given person's reaction to that vaccine, are quite common. Stelwagon,[2] in the Chairman's address before the American Medical Association in 1902, classified these rashes as follows:

Local:	Local Erythema Dermatitis Local Vaccinia Adenitis
Systemic:	More Generalized Erythema (Roseola Vaccinia) Urticaria Erythema Multiforme Vaccinia Generalized Purpura

Purpura is very rare. Fox, in a discussion of Malcolm Morris's paper [3] on vaccination eruptions, read before the British Medical Association in 1890, said, "The rare purpura is of ill omen."

The following case report is one of such an eruption—a patient, who, following vaccination, presented the symptoms characteristic of purpura of the thrombocytopenic type.

REPORT OF CASE

History.—P. K., a boy, Greek, aged 7 years, had been seen several times in the last four years in the outpatient department of the Milwaukee Children's Hospital. At no time did he show any symptoms of purpura. On account of

* Received for publication, Aug. 4, 1925.

1. Koehler, J. P.: Personal communication.

2. Stelwagon, H. W.: Concerning Some Vaccinal Eruptions, J. A. M. A. **39**:1291 (Nov. 22) 1902.

3. Morris, Malcolm: Brit. M. J. **2**:1229, 1890.

persistent enlargement of his tonsils, their removal had been advised. On Feb. 20, 1925, ten days after vaccination, he was admitted to the hospital on account of a profuse nose bleed. The bleeding had started three days after vaccination on his left arm. It was followed by the appearance of numerous fine petechial hemorrhages surrounding the vaccination area.

Examination at the time of admission showed a well developed, pale child, not acutely ill. The temperature was 100.2 F.; the pulse ranged from 100 to 110, and respiration was 24. The mucous membranes were pale. The nose had been packed with gauze. On the removal of the gauze, several hemorrhagic areas were visible on the middle turbinate and septum of the left nostril. The pharynx was slightly reddened and the tonsils were hypertrophied. The cervical lymph nodes were slightly enlarged. The heart and lungs were apparently normal. The spleen was not palpable (several examinations)). The entire skin surface, particularly that of the extremities, showed ecchymotic areas in various stages of color change. The capillary resistance test was positive.

Blood Examination.—Red blood cells, 3,100,000; white blood cells, 7,600; hemoglobin, 70 per cent. (Tallqvist). Differential count: Polymorphonuclears, 72 per cent.; small lymphocytes, 18 per cent.; large lymphocytes, 5 per cent.; endothelial leukocytes, 4 per cent.; eosinophils, 1 per cent. Coagulation time: capillary tube method, three minutes; Howell method, four minutes. Bleeding

Summary of Blood Picture

Date	Coagulation Time	Bleeding Time	Blood Platelets	Clot Retraction	Capillary Resistance
2/21	3 minutes	32 minutes	60,000	None in 24 hours	Positive
2/23	Transfusion of 250 c.c. whole blood (paraffin tube)				
2/25	3 minutes	3 minutes	.....	.....	Positive
2/26	.....	.....	80,000	.....	Positive
2/28	.....	.....	100,000	.....	Positive
3/ 2	.....	.....	110,000	.....	.....
3/ 3	3 minutes	3 minutes	.....	5 hours	Positive
3/ 4	.....	.....	120,000	.....	.....
3/11	3 minutes	5 minutes	130,000	6 hours	.....
3/18	.....	.....	.....	.....	Positive
3/25	4 minutes	5 minutes	140,000	4 hours	.....
4/13	3 minutes	4 minutes	130,000	5 hours	.....

time, thirty-two minutes. Platelets, 60,000 (Wright-Kinnicutt). There was no clot retraction in twenty-four hours. The Wassermann reaction and blood culture were negative.

The nasal bleeding continued fitfully after admission, so that on February 24 the child was given a transfusion of 250 c.c. of whole blood by Dr. Stanley Seeger. The blood was given by the paraffin tube method.

The table exhibits the gradual increase in the number of platelets, as well as the shortening of the bleeding time and return of the normal clot retraction after transfusion. It is noteworthy that while the bleeding time and clot retraction show immediate change, the platelet count exhibits a much less striking response and the capillary resistance test practically no response to the transfusion. One month after the patient's acute symptoms had subsided, the capillary resistance test was still positive. Two months after these symptoms, the platelet count was still comparatively low.[4]

So far as the subjective symptoms were concerned, the child made an uneventful recovery, and had no further hemorrhages either during his remaining stay in the hospital or subsequent to discharge.

4. The normal platetelet count in this hospital, as done in frequent determinations by a standard Wright-Kinnicutt technic by the same technician, averages from 200,000 to 300,000.

COMMENT

The symptoms and signs on admission were those established as diagnostic criteria for purpura hemorrhagica of the thrombocytopenic type. These symptoms and signs are the occurrence of bleeding, associated with the following hematologic picture:

Normal coagulation time; prolonged bleeding time; low platelet count; delayed clot retraction; positive capillary resistance test.

A perusal of the literature of the last few years leaves one confused as to the essential nature of this disease. Particularly obscure are the attempts at classifying it pathogenically. While some investigators would ascribe its various manifestations to the number and integrity of the platelets, others attribute more importance to the endothelial lining of the vessel wall. Still others regard these two factors of reciprocal significance.

It is, therefore, difficult to explain the present instance of the disease. Its occurrence following vaccination is unusual. While no specific relationship could be demonstrated, the sequence is interesting. Nocke,[5] in reporting a similar case in 1921, called attention to the analogy of the phenomenon to the low platelet count in purpura variolosa. The rarity of purpura following vaccination challenges the premise of such analogy. The well known pathologic changes responsible for the purpuric manifestations of variola do not obtain in either case.

418 East North Avenue.

5. Nocke, H.: Monatschr. f. Kinderh. **19**:455 (March) 1921.

Abstracts from Current Literature

Anatomy and Physiology

MICROSCOPICAL OBSERVATIONS ON THE CIRCULATION OF THE BLOOD IN THE CEREBRAL CORTEX. HOWARD FLOREY, Brain **48**:43-64, 1925.

The author discusses a microscopic method for the examination of the cerebral cortex. Experiments were performed on cats, rabbits and one monkey. Florey applied Krogh's methods to investigation of cerebral circulation. He describes the technic minutely, also the thrombus formation and the early stages of meningitis. It was found that cerebral arteries reacted to mechanical, thermal, electrical and chemical stimuli by contraction and dilatation, and the arterial ends of the capillaries also showed this ability to contract. Florey observed no evidence of nervous control over the caliber of the cerebral vessels. He concludes that "the inflammatory changes observed in regard to the cortical vessels are essentially the same as those occurring in a region supplied with vasomotor nerves."

PHYSIOLOGIC STUDIES ON THE PATELLAR REFLEX, I. THE PATELLOMETER. J. R. PEREIRA, Brain **48**:255-258, 1925.

The author cites evidence for and against the belief that the knee-jerk is a true reflex. As against, that the contraction curve of the quadriceps muscle resembles a simple twitch as opposed to the well established fact that all reflex contractions are of a tetanic nature, and also that the latent period of the knee-jerk is shorter than that of most reflexes. He quotes the work of Sherrington and Jolly against these arguments. The author states that the form of muscular contraction has not been satisfactorily explained as single twitches, double contractions with clonic and tonic phases and curves with oscillatory shapes are found in normal persons and described as normal types of muscular contraction. He believes that the latent period and form of muscular contraction are not reliable indications of the condition of the nervous centers governing knee-jerks. Pereira, believing that a new series of investigations on patellar reflex would take "into consideration the threshold of excitation, that is, the minimum intensity of stimulation necessary to produce the first perceptible response," designed an instrument called the "patellometer" for this purpose. The picture and method of working are described.

OLIGODENDROGLIA AND ITS RELATION TO CLASSICAL NEUROGLIA. WILDER PENFIELD, Brain **47**:430-452, 1924.

Penfield discusses at length, with illustrations, the group of adventitial cells separated by Cajal from neuroglia under the name of "third element," composed, as shown by Del Rio-Hortega, of oligodendroglia and microglia. He groups the interstitial cells of the central nervous system as follows:

Interstitial Cells	In White Matter	In Gray Matter
1. Neuroglia, classical (ectodermal).....	Fibrous.....	Perineuronal (satellite)
2. Oligodendroglia (probably ectodermal).	Interfasicular.....	Present and numerous
3. Microglia (probably mesodermal).....	Present (no subdivision)	Protoplasmic (no subdivision)

He states that the function of the oligodendroglia cells is not settled, but it seems probable "that they have to do with the elaboration and maintenance of myelin."

A Study of Fifteen Hundred Chinese Blood Groups. Li Chi-Pan, Nat. M. J., China **10**:252-261, 1924.

The author used the microscopic hanging drop method for 600 of his tests, and Vincent's open slide method and Jansky's classification for 900. His results are as follows:

	Blood Group				
	I	II	III	IV	Total
Number	470	571	310	149	1,500
Percentage	31.3	38.1	20.7	9.9	100

The author found the blood groups in China quite different from those of other races.

He states that isohemagglutinins are thermostable, normal to man and usually not developed until about six months after birth.

He tested out seventy-two Chinese children with the following results:

Age	Cases Tested	Red Cells Agglutinable	Red Cells Nonagglutinable
From birth to 1 month	8	62.5%	37.5%
1 month to 6 months	7	71.4%	28.6%
7 months to a year	3	66.6%*	33.3%*
1 year to 2 years	14	85.7%	14.3%
3 years to 4 years	5	40.0%*	60.0%*
5 years to 6 years	3	33.3%*	66.6%*
7 years to 8 years	12	75.0%	25.0%
9 years to 10 years	20	75.0%	25.0%

* Variation of percentage is probably due to an insufficient number of cases listed.

Agglutinin and agglutinogen appear, if they are ever to do so, before the child reaches 6 months, and when once developed their characteristics are permanent throughout life.

Lucas, San Francisco.

Pathology, Bacteriology and Biochemistry

Studies on the Biology of the Streptococcus Erysipelatis. I. Agglutination and Agglutinin Absorption with the Streptococcus Erysipelatis. Konrad E. Birkhaug, Bull. Johns Hopkins Hosp. **36**:248, 1925.

Intracutaneous injection of agar inoculated with live *Streptococcus hemolyticus* for the production of immune bodies was found to produce an immune serum of a higher agglutinin titer than that obtained by the intravenous or subcutaneous inoculation of dead or live hemolytic streptococci.

Of 34 strains of erysipelatous hemolytic streptococci, seven were employed for the production of seven immune erysipelatous serums. Thirty-one strains of the thirty-four erysipelatous strains, or 91.2 per cent., agglutinated with each of seven immune erysipelatous serums.

Of 45 strains of hemolytic streptococci isolated from sources other than erysipelas, nine or 20 per cent., were agglutinated by several immune erysipelas serums. Eight of the nine strains of *Streptococcus hemolyticus*, which were agglutinated by the serum from rabbits immunized against erysipelatous strains, were obtained from cases of nasal sinusitis.

Agglutinin absorption was accomplished under the conditions of the experiments, with all the combinations of immune erysipelatous serums and strains of hemolytic streptococci of erysipelatous origin.

These experiments indicate that it is possible to differentiate by immunologic methods a group of hemolytic streptococci causing erysipelas from the group of hemolytic streptococci responsible for scarlet fever, on the one hand, and on the other, from large series of miscellaneous hemolytic streptococci producing a variety of pyogenic infections.

Lyttle, New York.

ON THE SPECIFICITY OF THE SO-CALLED ARSENIC RECEPTOR IN THE HIGHER ANIMALS. CARL VOEGTLIN, HELEN A. DYER and C. S. LEONARD, J. Pharmacol. & Exper. Therap. **25**:297 (May) 1925.

In a previous paper Voegtlin and his co-workers have presented experimental evidence, showing that the action of arsenicals on protoplasm is essentially due to a union with certain organic sulphur compounds, containing the sulphur in the mercaptan form (sulphydryl). The toxic action of organic oxids of trivalent arsenicals is neutralized by the administration of organic sulphur compounds containing the SH group.

In this paper they present experimental evidence that glutathione, in adequate dosage, administered to a rat before or soon after the injection of from one to one and a half minimal lethal doses of arsenoxid, protects the animal completely. When a mixture of glutamic acid and cystin is injected in place of glutathione, the animals are also protected, but if cystin alone is given they do not survive the injection of the arsenic compound. Sodium thiosulphate also exerts some protective action, but not sufficient to enable the rat to recover from the effects of the drug.

The authors, therefore, suggest that the toxicity of arsenoxid is due to asphyxia of the cells, which occurs when the SH group of the glutathione combines with the organic arsenical. When glutathione is injected in sufficient amount, it binds the organic arsenic compound, thereby protecting the cells from the toxic action of arsenical. They suggest the administration of glutathione in arsenic poisoning.

THE EFFECT OF THE ADMINISTRATION OF DESICCATED RED BONE MARROW AND SPLEEN ON THE RESISTANCE OF ERYTHROCYTES TO HYPOTONIC SALINE SOLUTION IN DOGS. CHAUNCEY D. LEAKE and EMMETT F. GUY, J. Pharmacol. & Exper. Therap. **25**:357 (June) 1925.

The authors observed a rise in the number of circulating erythrocytes following the administration of red bone marrow and spleen. The increase in the number of reticulocytes was inadequate to explain this; they therefore studied the resistance of the red blood cells to hypotonic salts solution, using the technic described by Simmel. They found a striking increase in the osmotic resistance of erythrocytes to hypotonic saline solutions after the administration of desiccated spleen and red bone marrow to dogs.

THE BINDING POWER OF SERUM FOR DRUGS TESTED BY A NEW IN VITRO METHOD. R. BEUTNER, J. Pharmacol. & Exper. Therap. **25**:365 (June) 1925.

Beutner studied the binding power of serum for drugs, including pilocarpin hydrochlorid, atropin, morphin and strychnin, using for this purpose the method of dialysis through collodion. Some of the drugs when added to serum failed to dialyze, while others dialyzed to a variable degree. A drug which is completely bounded by the serum of one animal may remain free in the serum of another animal. Heating the serum to 65 C. seems to alter its binding power.

BLOOD CHEMISTRY IN ACUTE HISTAMINE INTOXICATION. HIROTOSHI HASHIMOTO, J. Pharmacol. & Exper. Therap. **25**:381 (June) 1925.

Hashimoto studied the chemical changes in the blood of dogs, following the administration of large doses of histamin. The shocklike condition lasted from three to five hours, during which time an increase in the nonprotein nitrogen, and urea nitrogen in the blood was observed. There was no consistent change in the chlorids or bicarbonate of the plasma.

FURTHER STUDIES ON THE EFFECT OF IODIDES ON THE HUMAN NITROGEN METABOLISM. G. P. GRABFIELD and A. M. PRENTISS, J. Pharmacol. & Exper. Therap. **25**:411 (June) 1925.

The authors studied the effect of the administration of iodids on the nitrogen metabolism. They had previously shown that iodids increase the nitrogen of the urine of patients on a fixed protein intake.

In this paper they present evidence to show that sodium, lithium, strontium and magnesium iodids have an immediate effect, whereas with the calcium and potassium salts, the increase in nitrogen output is delayed. The nonprotein nitrogen of the blood falls, when the nitrogen elimination in the urine rises. If the excretion of nitrogen is delayed, the nonprotein nitrogen accumulates in the blood.

IS INSULIN AN UNSTABLE SULPHUR COMPOUND? JOHN J. ABEL and E. M. K. GEILING, J. Pharmacol. & Exper. Therap. **25**:423 (July) 1925.

The authors attempted to isolate insulin. The ultimate aim was not attained, but they did obtain a fraction which was about three and one half times as powerful as the original material (insulin-Lilly). This purified fraction contained neither phosphorus nor ammonia, but did contain a large amount of a labile form of sulphur. The amount of sulphur seemed to be roughly proportional to the hypoglycemic effect of the purified extract.

The authors intimate that the amount of labile sulphur in insulin may eventually be used as a measure of its activity. They indulge in some suggestive speculations; namely, the possible relationship between sulphur compounds in the diet, and the elaboration of insulin by the islands of Langerhans, and an inadequate amount of sulphur in the diet and the development of diabetes mellitus.

A method for determining the amount of labile sulphur is described in detail. The work is being continued.

THE LIBERATION OF ABSORBED SUBSTANCES FROM PROTEINS. A FUNCTION OF THE BILE SALTS. SANFORD M. ROSENTHAL, J. Pharmacol. & Exper. Therap. **25**:449 (July) 1925.

Rosenthal has made the interesting observation, that bile salts liberate dyes, such as rose bengal, phenolsulphonephthalein, and bromsulphonephthalein, from substances to which they are bound in serum. In the case of the first two substances mentioned, the binding is complete, because none of the dye is to be found in the filtrate, when filtration of serum under pressure through collodion is carried out before the addition of bile salts. When bile salts are added a considerable amount of the dye appears in the filtrate. In the case of phenolsulphonephthalein, part of the dye seems to be free, and part bound. The addition of bile salts to the serum increases the amount of free dye. Bilirubin is also freed from its combination in serum by the addition of bile salts.

KRAMER, Baltimore.

BONE-MARROW INVESTIGATIONS IN NURSLINGS. EUGEN KRAMER and VALERIE HENSCH, Monatschr. f. Kinderh. **30**:440, 1925.

On this study the authors introduced a sharp trocar with a 1 mm. needle, about the size usually employed for artificial pneumothorax, into the cavity of the tibia. The point selected was on the medial surface just below the

tuberosity. As with lumbar puncture the entrance of the needle into the cavity is recognized by the sudden cessation of resistance. The trocar was then withdrawn and a sterile syringe used to aspirate a few drops of the contents of the cavity. A smear was then made and studied as if it were a blood preparation. The results of this study are of considerable interest.

The conclusions reached are as follows:

The bone marrow of infants is approximately 61 per cent. leukocytes and 25 per cent. lymphocytes. Basophils average below 1 per cent., and eosinophils from 1 to 3 per cent. Of the lymphocytes the small mononuclears predominate.

To 100 leukocytes are about five to ten nucleated red cells. Of the red cells, those with rod-shaped nuclei appear in greater numbers than in the blood. In syphilis the percentage of nucleated red cells may rise to from 24 to 47 per cent., and in rickets from 15 to 20 per cent.

In diseases associated with blood leukocytosis, changes in the bone marrow, in view of the already existing leukocytosis, are not so marked.

GERSTLEY, Chicago.

THE SECRETION OF HYDROCHLORIC ACID IN NORMAL CONDITIONS AND IN CHRONIC GASTRIC AFFECTIONS OF CHILDREN. GRETA MUHL, Acta Pediat. **4**:356 (Aug.) 1925.

Values for free and combined hydrochloric acid in the gastric contents of children are generally smaller than with adults. In normal children, variations from the usual picture are most uncommon. Hyperacidity has occasionally been observed in neurotic children, and in cases of peptic ulcer. Hypochylia or achylia may develop as a result of acute infections or chronic gastric disorders and may last for a long time. Two cases of achylia appeared to be congenital in origin.

HOLT, Baltimore.

Nutrition

GASTRO-INTESTINAL DISTURBANCES IN INFANTS AS A RESULT OF OBSCURE INFECTION IN THE MASTOID. ARTHUR M. ALDEN and HARRY W. LYMAN, Laryngoscope **35**:586, 1925.

A close relationship between infections of the middle ear and gastro-intestinal disorders has been found by Alden and Lyman to exist in many cases. Such a relationship is frequently overlooked, however, or recognized too late to save the child's life. Renaud, in 1921, examined the middle ear and mastoid in seventy consecutive necropsies on infants that had died from athrepsia and infantile diarrhea. In all of them extensive suppuration in the middle ear and mastoid antrums was found. Thirty cases had been diagnosed as otitis media during life, while the remaining forty had been overlooked. The final diagnosis in practically all the cases was infantile diarrhea. In the author's experience with a series of these conditions, they found that examination of the ears of these infants rarely shows the conventional signs of acute suppuration in either the middle ear or mastoid, and in none of their cases was any of the external signs of mastoiditis present. The drum membranes always show some change in color, the normal luster having given place to a dirty gray, opaque appearance. A distinct sagging of the posterior superior wall of the auditory canal is a frequent finding.

Ordinary incising of the drum membrane is often insufficient in these cases, due to the large amount of soft mesodermal tissue in the antrum, attic and

upper portion of the middle ear which swells and prevents these cavities from draining out through the canal. Also, in order to insure good drainage, the incision must include not only the upper portion of the tympanic membrane but also the membranous floor of the mastoid antrum as well, for in infants the tympanic annulus in its superior portion is incomplete, thus causing a bulging downward of the antrum floor from any accumulation of fluid in that cavity. The authors advise an early operation on the mastoid rather than temporizing with more conservative measures, as heretofore the mortality rate in this condition has been 100 per cent., while in their series, by early surgical intervention, they reduced the mortality 50 per cent.

SNAPP, Grand Rapids, Mich.

DEFICIENCY DISEASES OF CHILDREN. FREDERICK F. TISDALL, Canad. M. A. J. **15**:904 (Sept.) 1925.

Rickets, tetany and scurvy are discussed under this heading. The cardinal symptoms of these diseases are reviewed.

The author believes that the most important phase of rickets is the general lowering of resistance to infection. He also states that emulsions of cod liver oil are of no value in the treatment of rickets and that in his experience the pure cod liver oil, especially the Newfoundland cod liver oil, is the only one of value.

No new facts are brought out in regard to any diseases discussed. The main point brought out is that these are preventable diseases and will not develop, if cod liver oil, sunshine and orange juice are given early, regularly and in suitable doses.

MOORE, Omaha.

THE TREATMENT OF ACUTE DIARRHEA IN INFANCY. G. B. ALLARIA, summary of four articles appearing in La Prat. Pediat. for March, April and May, 1925.

To prevent the occurrence of acute diarrhea in infants the author urges:

1. Minimal changes in diet.

2. Protection against excessive atmospheric heat; careful regulation of room temperatures; use of light clothing; increased bathing during the summer months; removal, when possible, to cooler climate during the very hot months.

3. Vigilance and caution in the preparation and preservation of foods and accessories (nipples, etc.).

When the diarrhea occurs, treat each patient individually and gage therapeutic procedures prudently.

Besides the strictly dietetic treatment, Allaria discusses at length direct remedies (purgatives, antemetics, intestinal antiseptics, astringents, carminatives) and auxiliary measures (stimulants, regulators of body heat, digestive correctives, tonics, etc.). These, he believes, are important adjuvants in the treatment, but reliance should not be placed on them alone.

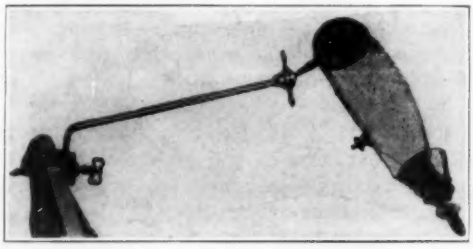
In the breast-fed if due to over feeding, too frequent feedings, or too great intervals between feedings, reduce the intake to six feedings in twenty-four hours. If this does not stop it, substitute water for the first morning feeding. Two or more such substitutions may be necessary in twenty-four hours. Return to the normal regimen gradually. If these measures fail, then antidiarrheic salts may be given when the normal milk diet has been restored. It is well, if bismuth salts are given, to warn the mother about stool changes that occur with this drug.

In bottle-fed babies the condition is usually more serious. Most of the fatalities attributable to acute diarrhea are in the artificially fed infant. The treatment, therefore, should be more rigorous. A liquid diet (water, only) should be given for at least twelve hours; if there is no improvement, increase to twenty-four hours. It is rarely necessary, and in fact is dangerous, to extend the liquid diet to forty-eight hours. Undernourished infants tolerate this very badly even for a few hours, so that breast milk should be given to these patients. When milk again forms the greater part of the diet, medications may be given as indicated. For severer cases, sugar, milk, and mucilaginous drinks are added; astringent drugs may be given. In older children, rigorous liquid diet is rarely necessary. Small doses of bismuth and opium may be given as indicated. Diet should consist essentially of gruels, soups, etc.

The author denounces the initial purge; he believes it serves no useful purpose and provokes irritation and vomiting, which tend to exaggerate the already increased peristalsis. Worse still is the prediagnosis purge.

A New Type of Nursing Bottle Holder. O. Cozzolino, La Prat. Pediat. **2**:95, 1925.

This holder can be attached to the ordinary crib, and is easily adjustable to any angle or height desired. The author claims that it insures a constant



and regular flow of milk, thus giving ample nourishment and prevents the ingestion of air. Infants easily become accustomed to it, and it saves a great deal of time for the mother.

Zambarano, Northville, Mich.

Observations on 1,057 Cases of Diarrheas in Infants. Rafael Duarte Salcedo, Arch. españ. de pediat. **9**:449, 1925.

The author concludes that the best prophylaxis against the high mortality from diarrheal disturbances lies in maternal education, and in systematic direction of the infants' feeding by the practitioner.

The most frequent cause of digestive disturbances lies in transgressions against the dietetic regimen, in improper feeding and in incorrect treatment. Therapy in diarrheal disturbances is influenced somewhat by the economic situation of the parents.

The milk station has not quite solved the problem in Spain. Its establishment in the outpatient services has not been successful.

The author believes that the possible relationship between dentition and diarrheal disturbances warrants further study.

In his opinion, the high infant mortality of Spain, while seemingly a reproach to Spanish pediatrics, lies in causes which are in many ways quite beyond their control. There is much confusion and disagreement among the profession gen-

erally as to proper methods of feeding and procedure in diarrheal cases, a good deal of it founded on lack of knowledge and error in judgment. The proprietary foods as usual play a prominent rôle in the drama, as they are widely used in Spain.

SCHLUTZ, Minneapolis.

COMPARATIVE OBSERVATIONS ON THE HEALING OF RICKETS. P. REYHER and M. SCHMAUCKS, Arch. f. Kinderh. **75**:161 (Feb.) 1925.

Thirty-five rachitic children were observed for long periods of time, under conditions which permitted a comparison of the effectiveness of the various antirachitic measures at present in general use. All children were on the same diet, which included milk and vegetables, but, in addition one group received heliotherapy in the form of sunlight, another cod liver oil, a third vitamins (a vitamin containing infant food, plus lemon juice or carrot juice of known potency), and the last (control group) received no therapy except an appropriate diet. Progress was followed by means of roentgenograms of the hand and the lower part of the arm, taken every two to four weeks. All patients showed healing tendencies in the summer months, this being most marked in the early summer (May to July) and least marked in late winter (January to March or April). Probably the reason for this seasonal variation is to be found in a greater antirachitic vitamin content of the milk and vegetables in early summer. Huldschinsky's much quoted experiments with ultraviolet rays were all undertaken in the months when there is normally a great tendency for rickets to heal, irrespective of therapy. How much sunlight therapy is overrated may be judged from the fact that certain infants of this series, who failed to improve in the sunlight, showed prompt healing when given a diet rich in vitamins. The most important factor in the production of rickets would seem to be a deficiency of vitamins in the diet, but the rôle of the fat soluble A substance is still problematical. It is possible, however, to influence the concentration of vitamins in breast milk and in cow's milk by means of diet, and the rickets of breast fed children can often be cured by appropriate changes in the mother's diet.

HEMPELMANN, St. Louis.

INCREASES OF TEMPERATURE OF THE LACTATING BREAST. KARL HEUSLER, Zentralbl. f. Gynäk. **49**:204 (Jan. 24) 1925.

After discussing the question of whether mothers of today are losing their ability to nurse their babies, the author cites the figures compiled by Martin, in 1920, which showed that in 1,000 cases only 0.8 per cent. were unable to nurse their babies. He states that while there are cases in which an absolute inability to nurse exists, there are many more in which at the beginning, or during the course of lactation, the milk secretion is maintained with difficulty or even suddenly ceases. The question arises whether a true, primary, hypogalactia or agalactia is present on an anatomic physiologic basis; or if from some other cause the breast function has not developed. The author then goes on to enumerate the numerous factors which may bring about a secondary hypogalactia; poorly developed nipples, cracked nipples, insufficient stimulation on account of harelip or cleft palate, or debility of the infant, etc.; and he reminds us that it is difficult to decide whether the hypogalactia in a given case is primary or secondary.

Moll found the temperature taken under the secreting breast to be from 0.5 to 0.8 C. higher than in the axilla, while in women who were pregnant, but not lactating, this was not the case, and often the reverse was true. The

increased temperature was found to be present even when the breast had been emptied by the nursing of the baby or by manual expression. When the breasts dried up, the difference in temperature gradually disappeared. In cases of hypogalactia in which the temperature of the breast was increased, it was an indication that the breasts were still functioning; and many a supposition of inability to nurse proved false. In women with fatty breasts with a small amount of gland parenchyma, the increase in temperature was not present and all attempts to bring about proper secretion failed.

The author's investigations were made on 176 women of which eighty-six were nursing their babies during the puerperium; ten were not nursing during the puerperium because their babies were dead; fifty were healthy women not nursing babies, and thirty were pregnant. Of the first group, all except one showed an increased temperature under the breast, while in the group of healthy nonnursing women, all but two showed either a lower breast temperature or a breast temperature the same as that in the axilla. In the group of pregnant women an increased breast temperature was present in about one half the cases during the eight to ninth month. In the group of ten mothers whose infants had died and the breasts were not stimulated, the breast temperature was at first higher than the axillary, and gradually fell, until by the tenth day post partum the breast temperature was lower than the axillary. In the one case of the first group in which the breast temperature was lower than the axillary, a primary hypogalacia was proved by the subsequent course of events. The author concludes that an increase of breast temperature over axillary temperature is a simple and accurate prognostic sign as to the functionability of the breasts.

PARMELEE, Chicago.

VITAMIN REQUIREMENTS OF MALNOURISHED CHILDREN. T. FROLICH, Acta Pediat. **4**:247 (Aug.) 1925.

The author believes that the baneful effects of artificial feeding can largely be attributed to lack of vitamins. In order to offset this he uses a concentrated milk feeding, adding malt soup (to supply vitamin B) and cod liver oil (to supply antirachitic factor). When the feeding is to be boiled, antiscorbutic substances are added also. Details of many cases illustrating the beneficial effect of this method of feeding are presented.

HOLT, Baltimore.

Prenatal Conditions

PLACENTAL TRANSMISSION. III. THE AMINO-ACIDS, NONPROTEIN NITROGEN, UREA, AND URIC ACID IN FETAL AND MATERNAL WHOLE BLOOD, PLASMA AND CORPUSCLES. E. D. PLASS and C. W. MATTHEW, Bull. Johns Hopkins Hosp. **36**:393, 1925.

The fetal and maternal whole blood and plasma from twenty normal patients at the time of delivery were analyzed for amino-acids, total nonprotein nitrogen, urea and uric acid. It was found that the amino-acid nitrogen is constantly higher in the fetal whole blood and plasma than in the maternal samples, thus confirming the investigations of Morse on plasma and of Bock on whole blood. The amino-acids, which are very probably necessary for the synthesis of proteins in the fetal organism, are thus seen to behave as do the other constituents, which are essential for growth (calcium and inorganic phosphates). It would seem that the preferment thus shown for the developing product of conception must be the result of the working of a definite

physico-chemical law, which acts to insure the fetus an overabundance of the essential "building stones." Simple diffusion does not explain the facts, and "selective absorption" is too indefinite to be of any value.

Largely by reason of this constant difference in the amino-acids and the established uniformity of the other nonprotein nitrogenous constituents in the circulations, the fetal whole blood and plasma were found to contain constantly more total nonprotein nitrogen than the maternal specimens. Such constant results have not been obtained by previous investigators, who came to the conclusion that these substances pass the placenta probably by simple diffusion. The urea and uric acid in the two bloods tend to be equal, and in all probability the slight differences detected at times may have been due to analytical errors. No definite relationship could be detected between the variations detected in the individual substances, and any facts obtained from clinical study of the patients.

They conclude as follows:

1. The amino-acids are uniformly higher in normal fetal whole blood and plasma than in the maternal.

2. The total nonprotein nitrogen is likewise always in higher concentration in the fetal whole blood and plasma.

3. Urea is usually found in equal concentrations in the two bloods.

4. Uric acid is usually found in equal concentrations in the two circulations, but, if there is a difference, it is generally higher in the fetal blood.

LYTTLE, New York.

INJURY OF THE CHILD AS A RESULT OF INTRA-UTERINE MANIPULATION. G. WINTER, Monatschr. f. Geburtsh. u. Gynäk. **70**:12 (July) 1925.

Winter has observed that if intra-uterine manipulation, such as version, is not followed by immediate delivery the babies do badly. These observations extended over a period of many years with consistent figures. In all, he has collected 634 cases of version.

Four hundred and ninety-four cases with immediate extraction resulted in twenty dead infants, a mortality of 4 per cent., while 123 cases of version alone gave a mortality of 50 per cent. This increase of mortality he attributes to various factors, such as insult to the umbilical cord, separation of the placenta or stimulation of the child resulting in attempts at breathing within the uterus.

It is noteworthy that in spite of the large series reported no necropsy findings are recorded and no reports on the state of surviving children. Even so, the facts appear to be definite enough to justify close attention to the time between version and delivery, in taking histories of children when birth injury is suspected.

CROTHERS, Boston.

Diseases of the New-Born

CONCERNING SUPRARENAL HEMORRHAGE IN THE NEW-BORN. S. JOSEPH and E. RABAN, Zentralbl. f. Gynäk. **49**:1 (Jan. 3) 1925.

Hemorrhages in the suprarenal glands as an accidental necropsy finding are frequently reported, but only a few cases have thus far been reported in which the hemorrhage was so extensive as to cause death. The authors report a case of a child born at term. The delivery was rather difficult, and the child was mildly asphyxiated but recovered without strenuous measures of resuscitation. Thirteen hours after delivery cyanosis appeared suddenly, and death

occured three hours later. At necropsy an extensive hemorrhage of the right suprarenal gland was found; there were no other findings, except a few small, superficial hemorrhages on the cerebral convexities. The authors conclude that venous congestion of the suprarenal, due to trauma during delivery, was followed thirteen hours later by hemorrhage, which finally ruptured the capsule and spread into the surrounding tissues.

PARMELEE, Chicago.

Acute Infections

RHEUMATIC HEART DISEASE. ERNST P. BOAS, M. Clin. N. Am. **9**:393 (Sept.) 1925.

The vague manifestations of rheumatic infections in early childhood have such serious possibilities that to wait for frank arthritis before recognizing them as such, may lead to irreparable cardiac damage. Anemia, irritability, fleeting muscular pains, preceded or accompanied by tonsillitis, pharyngitis, chorea or erythema multiforme, are frequently the only symptoms antedating the development of rheumatic carditis. The younger the child, the more indefinite are the symptoms likely to be, and the more probable the involvement of the heart.

The author feels that too much emphasis has been placed on the tonsil as the chief portal of entry of the rheumatic virus, and would incriminate, rather, the whole of the respiratory tract, especially its upper portion. Heredity as an important predisposing factor is shown by Cheadle's carefully taken family histories.

The author's attitude toward tonsillectomy as a prophylactic measure is made clear by the statement that in his experience "most tonsillectomies, whether on sufferers from heart lesions or on others, are unwarranted." "The evidence that removal of the tonsils will prevent recurrences of rheumatic infection is not convincing, and the operation is not so innocuous as many would have us suppose." The indications for tonsillectomy in patients with rheumatic heart disease are the same as in those with normal hearts, namely, repeated attacks of tonsillitis, badly infected tonsils with large tonsillar lymph nodes, and obstruction to respiration and deglutition. In case of doubt, postpone operation. The teeth should be cared for as a general health measure, and not with the idea of influencing directly the heart lesion.

THE DIAGNOSIS OF ACUTE RHEUMATIC PERICARDITIS. ROBERT A. LOEB, M. Clin. N. Am. **9**:455 (Sept.) 1925.

The simulation of an upper abdominal crisis by acute pericarditis is illustrated by the case of a youth, aged 16, who was admitted in considerable shock, complaining of very severe epigastric pain. His history was negative for tonsillitis, rheumatism, scarlet fever, chorea or any circulatory disturbance. Two weeks previous he had had a sore throat, accompanied by a dry cough, which persisted. A few days later he experienced rather sudden pain in the epigastrium, and vomited. The pain has continued in greater or less degree, and the patient experienced slight dyspnea on walking. A few hours before entering the hospital, he was awakened by more intense pain in the upper abdomen, aggravated by respiration. About the same time he noticed a blotchy rash on his arms. On admission, he was found to be pale, sweating, with shallow respirations and grunting expiration. Both sides of the chest expanded normally; the diaphragm was high and moderately fixed. There was slight enlargement of the heart to the right and left, and the apex beat was neither seen nor felt. No friction rubs were heard, and the heart sounds were slow,

regular and distant. The abdomen was slightly full and with no respiratory movement. There was "board like" rigidity above the umbilicus, with acute tenderness. The temperature was 102.4 F., pulse 78, respirations 30 and leukocytes 13,000. A diagnosis of perforated peptic ulcer was made on the history of indigestion for the last year, the sudden exacerbation of acute abdominal pain and the classical signs of peritoneal irritation. Operation revealed no abnormalities within the abdomen.

The next morning, a soft diastolic murmur was heard at the apex, and a suggestion of a pericardial friction rub to the left of the sternum and below the right nipple. On the second day a loud pericardial friction rub was audible over the greater part of the precordium, which persisted for one week. The temperature ranged from 98 to 103 F. At no time was there any precordial pain. Two years later the patient was well, with no abnormal physical findings except moderate enlargement of the heart and some mitral insufficiency.

Reference is made to three other cases of acute pericarditis, two in children of 6 and 10 years, in which the symptoms so closely simulated those of an acute abdominal condition that laparotomy was done.

An analysis of thirty-four cases of acute rheumatic pericarditis showed that the most characteristic signs and symptoms were fever, cough, dyspnea, moderate leukocytosis and precordial pain, all of which may precede the development of a pericardial friction rub.

MENINGOCOCCUS BACTERIEMIA. ARTHUR E. NEERGAARD, M. Clin. N. Am. **9**:461 (Sept.) 1925.

Two cases of meningococcus bacteriemia without demonstrable localizing lesions are discussed, and the following points in the clinical picture are emphasized:

1. A week or more of careful study and observation preceded the making of a correct diagnosis. Typhoid fever, influenza, malaria, septicemia and acute rheumatic fever were suggested and in turn were ruled out.

2. The organism fails to grow on glucose broth ordinarily used for blood cultures. Special mediums, such as blood broth or blood agar, are necessary for its recovery.

3. The temperature chart shows spikes which occur with no regular sequence, and there may be afebrile periods of from one to four days. The patients did not appear or feel particularly sick except at the height of the fever.

4. The skin eruption was maculopapular, sometimes hemorrhagic, simulating that of typhoid fever, measles or the toxic erythemas.

5. Fleeting joint pains were present in both cases.

SMITH, Ogden, Utah.

BACTERIOLOGICAL FINDINGS IN ACUTE DYSENTERY IN CHILDREN. GEORGE F. KLUGH, South. M. J. **18**:709, 1925.

The author presents a preliminary report on results of study of acute bloody dysentery in children.

Streptococci and the dysentery bacillus (Flexner type) seemed to be the chief causative factors.

To make an early diagnosis, gram stains and litmus lactose agar plate cultures are made from particles of bloody mucus.

Vaccination is advocated as a feasible prophylactic measure, especially during epidemics. Antidysentery serum gives good results if given early.

Theoretically, lactose and acidophilus milk seem to be ideal foods for dysentery patients, but any small amount of easily digested food is probably absorbed before it reaches the infected area.

SCHLUTZ, Minneapolis.

THE ORTHOPEDIC TREATMENT OF POLIOMYELITIS. J. REY, Arch. f. Kinderh. **75**:173 (Feb. 10) 1925.

A brief résumé (illustrated) is given of the orthopedic measures used to prevent and overcome the deformities resulting from poliomyelitis. It is especially important that the pediatrician, who sees these infants in the acute stage, realize his responsibility in preventing deformities due to contractures of the knee and hip flexors, foot drop, etc. Sometimes amazing restoration of function in an apparently badly paralyzed muscle results from correction of the contracture and taking the stretch off of such muscles. There are very few children who cannot be made to walk again by means of such measures as the correction of contractures, relief of stretching, tendon transplantation, arthrodesis, etc.

HEMPELMANN, St. Louis.

CLINICAL OBSERVATIONS IN AN EPIDEMIC OF VARICELLA. JOSEF HEUBERGER, Monatschr. f. Kinderh. **30**:385, 1925.

The mother of the child had an attack of typical herpes zoster. Two weeks later both she and her child suffered an attack of varicella. In her case, however, the eruption was not typical but consisted of maculopapules with relatively few vesicles. From that time, other children in the ward sickened, with an incubation period varying from ten to nineteen days.

In an effort to test the efficiency of vaccination against chickenpox, thirty-six children were inoculated with contents of the vesicles. A positive reaction was obtained in 25 per cent. of those inoculated. Of these, 77 per cent. did not contract the disease, while only 33 per cent. of the uninoculated escaped.

STUDIES ON VACCINATION. W. KUHLE, Monatschr. f. Kinderh. **30**:390, 1925.

The study is divided into four parts, containing observations on the general, the local, the intracutaneous and the subcutaneous reactions.

The general reaction consists of four stages. The first period, lasting from two to three days, shows usually a subfebrile temperature. In the second stage, during the fourth to seventh days, the fever gradually rises. The third stage, lasting until the tenth day, is the height of the reaction and passes over to the fourth stage in which the fever slowly subsides. Fever shows no relation to age, constitution, or local reaction. In the earliest stage there is leukocytosis at the height, leukopenia and later again leukocytosis, the cells being polynuclears. There are no other blood changes. In severe local reactions the adjacent lymph nodes are enlarged. In nurslings under 2 years the reaction is mild, the temperature being usually subfebrile.

As regards the local reaction there is little controversy. The papule appears on the fourth to the seventh day and by the eight to the tenth has become a pustule. On the twelfth day it starts to dry. Contrary to the usual idea the contents of the pustule are sterile. The turbidity is due to necrosis of the wall with wandering in of leukocytes, but in the normal case there should be no bacteria present.

Immunity may be achieved by intracutaneous inoculation, in doses varying from dilutions of 1:10 to 1:50. This method may be employed when haste in

securing immunity is necessary. In dilutions of 1:10 infiltration begins on the first day, and the reaction later may be severe enough to cause considerable vesicle formation. In order to avoid this the author tried dilutions of 1:50 and found this equally satisfactory in producing immunity, and the local and general reactions were not so severe.

Knopfelmacher has shown that in dilutions of 1:200 subcutaneous injections produce immunity. Kuhle's experiments confirm this. The local reaction in these cases consists of an erythema for the first day, a latent period until the ninth and then a considerable redness and some infiltration lasting until the twelfth.

At all times unless urgent speed is required or unless one is particularly desirous of avoiding a scar, the usual cutaneous method of vaccination is to be preferred.

GERSTLEY, Chicago.

DIETETIC TREATMENT OF DYSENTERY. R. STANKIEWECZ, Polish Pediat. **5**:34, 1925.

The author had good results in treating his patients with whey or buttermilk, gradually adding sugar, oatmeal, cow's milk or human milk. Good results have been obtained with Moro mixture (milk, flour and butter), 400 to 700 gm. a day.

INFECTIOUS JAUNDICE. MIKULOWSKI, Polish Pediat. **5**:39, 1925.

During 1924 there has been noted more frequently in children the appearance of catarrhal jaundice, with clinical pictures corresponding to that described by various authors as infectious jaundice. The disease started suddenly with high elevation of fever, and after two or three days' duration the fever dropped. Simultaneous jaundice persisted from one to four weeks. The disease could be observed in several children of the same family and in the schools in the same season. There was a child in the hospital, who, after a few days' contact with jaundiced patients, developed similar symptoms. The course of illness is mild.

PIOTROWSKI, Mansfield, O.

TREATMENT OF SCHISTOSOMIASIS. J. T. TAI, Nat. M. J., China **11**:158-165, 1925.

The great prevalence of *Schistosoma japonica* infection (lung fluke infection) along the Yangtze valley is emphasized (7 per cent. of the author's patients harbored this parasite and Faust estimated that 10,000,000 Chinese probably have it). Three drugs were tried out, sodium antimony tartarate, colloidal antimony preparations and emetin. He found the first the most efficient for this infection. Emetin, which is almost as effective, is to be preferred when there is any difficulty in intravenous injection, especially in children, and for prolonged treatment as it is better tolerated. Cure is impossible without intensive treatment for at least a month. One week's daily negative fecal examinations, preferably two weeks, indicates that the patient is rid of parasites.

LUCAS, San Francisco.

Chronic Infections

OBSERVATIONS ON CONGENITAL SYPHILIS. PHILIP HASKELL SYLVESTER, Boston M. & S. J. **193**:393-403 (Aug. 27) 1925.

This report is made from the medical service of the Children's and Infant Hospitals, Boston, and is given in connection with an excellent venereal disease symposium.

Of babies with congenital syphilis untreated or inadequately treated, 50 per cent. are dead at the end of the first year, 45 per cent. are below par physically and mentally, and 5 per cent. give promise of reasonable development. Syphilitic babies recognized as such in the first few weeks of life, when treated early and adequately, show hardly any greater mortality and morbidity than average run of outpatient babies.

After suggestive incidents in the family history are pointed out, the most frequently seen lesions are given and discussed, including: (1) skin and mucous membranes, (2) mucous membranes and mucocutaneous junctions, (3) viscera, (4) skeleton (roentgen-ray illustrations), (5) peripheral nervous system, (6) central nervous system, (7) organs of special sense, (8) lymphatic system and (9) general, or symptomatic. Late lesions (so called) are also discussed.

The treatment includes the use of one or more of the following drugs: mercury, iodids, arsphenamin, neo-arsphenamin and sulpharsphenamin, with preference for the latter judging by the results in the past two years. It is usually used as follows: Sulpharsphenamin is given intramuscularly to very young or very small babies in a dose of 0.05, 0.075 or even 0.1 gm., according to size and weight of the baby, for three doses, then increased by 0.05 gm. in each succeeding series of three doses until the baby has received a total of twelve doses at weekly intervals. At the end of this first series, the baby is given a vacation of one month, after which it returns for a Wassermann test. If this is negative, as it usually is, the baby is given a second series of twelve injections, each of about one half the corresponding dose of the previous series, when another month's vacation is given and a Wassermann test taken. If this is negative (as it has never failed to be in this group), the baby returns for blood test alone at the increasing interval of three months, six months and one year. In this group of young babies, of all those whose reactions have once become negative they have remained so to date. A small baby, critically ill with syphilis, or a syphilitic baby, critically ill with anything else, or in a state of severe malnutrition, is treated by mercury alone in inunctions or by a constantly applied binder, until its general condition has been improved to a reasonable degree. Then it is given sulpharsphenamin in small doses (0.05 to 0.075 gm.) at weekly or fortnightly intervals, meanwhile, the mercury being continued. When the baby is in really good condition the full course of twelve injections is given as above. In older children, the dose is started at 0.2 gm. and is rapidly run up to 0.4 gm. for a total of twelve weekly injections, and the series is repeated with a vacation of one month at the end of each series until the Wassermann reaction becomes negative. "So far we have had no general reactions, whatever, and no local reactions worth mentioning. To one who has seen the severe general reactions following the intravenous use of neo-arsphenamin, and who has been through the shrieking bedlam of a clinic in which it was being given intramuscularly, the peace, quiet and friendly atmosphere of the sulpharsphenamin clinic are very pleasing." It is Sylvester's hope and belief that the ease of preparation, simplicity and painlessness of administration and absolute freedom from severe reaction will make the comfortable and effective treatment of congenital syphilis possible and convenient in the hands of every general practitioner.

The following contraindications to the administration of arsenic are recognized: (1) in grave malnutrition from any cause, even syphilis; (2) in any severe infection, particularly of the lungs, as pneumonia or severe bronchitis; (3) in high fever from any cause; (4) in the presence of acute meningeal symptoms; (5) in nephritis.

While neo-arsphenamin may be safely given intramuscularly in small doses under any of the foregoing circumstances, it is probable that the rapid absorption of sulpharsphenamin makes its intramuscular administration just as dangerous as when given intravenously.

"A baby recognized and treated early, that is to say within the first six or eight weeks of life, will give a negative Wassermann reaction at the end of twelve injections and will continue to do so for a year and three quarters. A baby from 4 to 6 months old, treated likewise, may die in spite of treatment, will be under par mentally and physically for many months and may not give negative serum reactions for a year or more. His chances of coming out of the battle unscarred are pretty poor. In the older child, the expectation of obtaining a negative blood within two or three years is distinctly optimistic. Destructive bone lesions will require a year or two or even longer for complete repair. Hypertrophic and deformative bone lesions have been unaffected by any treatment whatever, within the period of my observation. Clinical improvement, regardless of roentgenograms or serum reactions, is striking. Even the 'latent' cases gain weight, color and activity, and approach par mentally."

Some detailed results of therapy with sulpharsphenamin alone are also given.

THE SANATORIUM TREATMENT OF JUVENILE TUBERCULOSIS. COLE B. GIBSON, Boston M. & S. J. **193**:457 (Sept. 3) 1925.

Important to further control and prevention of tuberculosis are (1) continued study of the germ itself; (2) study of the various manifestations of the disease produced by the germ, and (3) educational dissemination of the results of these studies. In the treatment of juvenile tuberculosis, the sanatoriums have the following advantages:

1. Possibility of accuracy of classification for treatment. That is, only the active cases are cared for; the latent and inactive cases are discharged to home, clinic or school supervision.

2. Ease of individual treatment in conjunction with group management.

3. Coordination of treatment with continuance of education.

4. Therapeutic discipline. The child is taught to take his treatment methodically, when so often elsewhere sick or ailing children are permitted to follow therapeutic routine at their own discretion, solely because they are sick and ailing.

5. The applications of special methods of treatment may be better carried out in a sanatorium than elsewhere. This is especially true in artificial pneumothorax, postural rest, treatment by roentgen, clinical, electrical and solar rays, and tuberculin treatment.

6. The dietary, a most important part of the plan, can be scientifically devised and yet maintain tastiness and attractiveness.

7. All types of active tuberculosis of childhood may be treated in sanatoriums; pulmonary adult type, pulmonary juvenile type, bone, glandular, skin, abdominal and others of the less frequently encountered varieties. In a general way, the treatment of all is similar; certainly the fundamentals are identical: fresh air, good food, proper rest and sunlight. Medicinal therapeusis occupies no higher level of importance in children's sanatoriums than in those devoted to adults.

The Rollier treatment of gradual exposure to sunlight is used in all cases, except in the presence of hyperpyrexia or during acute intercurrent illnesses.

Localized heliotherapy, or the application of sunlight to a specific lesion or to a certain part of the body is not practiced. The treatment is not discontinued on dull days.

In patients with definite lung disease, extra caution is used, and the sunlight treatment is discontinued whenever signs of improper reactions are observed. In children who fail to tan properly, the administration of the tincture of the chlorid of iron, or painting with a weak solution of tincture of iodin, in conjunction with sunlight exposure will often be followed by pigmentation and improvement.

GENGENBACH, Denver.

TWO CASES OF TUBERCULOUS PERITONITIS WITH ASCITES CURED BY PNEUMOPERITONEUM. A. F. CANELLI, La Prat. Pediat. **2**:39, 1925.

The author reports two cases of tuberculous peritonitis with ascites. All ordinary methods of treatment failed. In one child, aged 4 years, frequently repeated abdominal tapping revealed an increasing amount of fluid. Eight hundred cubic centimeters of air were injected into the peritoneal cavity in divided doses. Recovery has been complete to date (three years after).

The second child, aged 6 years, had numerous tappings and a laparotomy with no improvement. Pneumoperitoneum was performed, and the child is now well two years after the treatment.

Both patients had an intensive course of heliotherapy following the injections of air. There were no complications and no shock was observed in either case.

STATISTICAL SURVEY OF CONGENITAL SYPHILIS. MADON and PORRERA, La Prat. Pediat. **2**:95, 1925.

All cases of congenital syphilis seen in the University of Torino Clinic from 1911 to 1924 were studied. The authors report:

1. That there has been an increase in its occurrence since the World War.

2. That one-half of the infants born of syphilitic parents die before or shortly after birth. Of the remaining half, about 50 per cent. show positive signs of syphilis during the first year of life. Many, however, do not show evidences of syphilis until after the second year.

3. That rarely does a child of syphilitic parents escape the stigmas of the disease completely.

Knowledge of the absolute, probable, and rarer signs of congenital syphilis is necessary, so that by early recognition efficient therapy may be instituted, both for the infant and for the parents.

The cardinal and suspicious signs are described in detail.

RELATION OF NERVOUS VOMITING IN INFANTS TO CONGENITAL SYPHILIS. L. GRANTINI, La Prat. Pediat. **2**:95, 1925.

Habitual vomiting in infants is rarely due to intolerance to milk; hereditary neuropathic tendencies may cause it; congenital syphilis is very frequently responsible.

A change in diet will cure the first type; symptomatic treatment is of considerable value in the second type, and the syphilitic class responds well to specific therapy.

In frequent vomiting, when the cause is obscure, the thought of congenital syphilis as a possible factor is often of great value, and the author reports several instances in which beneficial results have followed proper management along syphilitic lines.

ZAMBARANO, Northville, Mich.

DIFFERENT REACTION OF TWINS TO CONGENITAL SYPHILIS. OSCAR HERZ, Monatschr. f. Kinderh. **30**:467, 1925.

A report is given of twins in which the girl showed all the symptoms of congenital syphilis and the boy did not. At the age of 3 months the boy contracted pneumonia and died. An extensive necropsy failed to reveal any signs of syphilis macroscopically or microscopically.

GERSTLEY, Chicago.

DIAGNOSIS, PROPHYLAXIS AND TREATMENT OF CONGENITAL SYPHILIS. E. KLAFTEN, Zentralbl. f. Gynäk. **49**:30 (Jan. 3) 1925.

The necessity for an accurate and early diagnosis by means of a simple method is stressed; and the value of the Meinicke clouding reaction and the Wassermann reaction of the serum from the umbilical cord, as well as the demonstration of spirochetes in the fetal end of the cord by dark field illumination and the demonstration of characteristic changes in the umbilical cord by microscopic examination of sections, are spoken of as some of the means we have at hand for making an early diagnosis in doubtful cases. Positive findings by any one of these methods are sufficient criteria to warrant the institution of active antisyphilitic treatment, even though the child at birth shows no sign or symptom of syphilis.

TABLE 1.—*Syphilitic Mothers Excepting Those with Latent Syphilis*

Condition of Child	Untreated Secondary 17 Cases	Tertiary 6 Cases	Congenital 3 Cases	Metasyphilitic 5 Cases
Healthy	0	6	3	5
Syphilitic	6	0	0	0
Macerated	11	0	0	0

TABLE 2.—*Cases of Latent Syphilis*

Condition of Child	Untreated 162 Cases	Treated		
		18 Cases Before Pregnancy Only	12 Cases Before and During Pregnancy	6 Cases During Pregnancy Only
Healthy	53	0	12	4
Syphilitic	38	4	0	2
Premature; no evidence of syphilis	0	1	0	0
Mentally deficient	0	1	0	0
Macerated	71	13*	0	0

* Twins in one case.

It is sometimes difficult to decide to institute treatment when a syphilitic mother gives birth to an apparently healthy child, even though we know that a relatively large proportion of these show signs of syphilis before the end of the first year. It is especially difficult to decide as to the necessity of treating those apparently healthy infants born of latent syphilitic mothers, who also show no signs of syphilis at the time of observation. The author presents two tables to show the results of his studies of cases in which the mothers were treated or left untreated, and concludes that the best prophylaxis of congenital syphilis is early diagnosis and thorough treatment of the syphilitic mother, before and during pregnancy, and recommends energetic treatment of children apparently healthy at birth, if the mother had secondary syphilis or untreated latent syphilis; also, if the mother were infected during pregnancy, even though she had been treated.

PARMELEE, Chicago.

THE RELATION BETWEEN ASTHMA AND TUBERCULOSIS. ARVID WALLGREN, Acta Pediat. **4**:286 (Aug.) 1925.

As a rule, the author finds that pulmonary tuberculosis and asthma are totally unrelated conditions. He reports, however, several cases of mediastinal tuberculosis which developed typical asthmatic attacks during a period when signs of bronchial compression were present. Since these asthmatic attacks did not respond to epinephrin and were not associated with eosinophilia, he feels that they cannot be classed with the ordinary asthmatic attacks due to constitutional idiosyncrasies. He attributes them to pressure on the sensory fibers of the vagus.

HOLT, Baltimore.

DIAGNOSTIC VALUE OF THE ERECTION SIGN IN TUBERCULOUS MENINGITIS. E. FLATAU, Polish Pediat. **5**:10, 1925.

The symptom of erection described by Dr. Flatau, in 1923, has a value of some importance. As it occurs quite exclusively in the terminal stage of tuberculous meningitis, it is of some help in the diagnosis of doubtful cases and of their prognosis. The paper is illustrated by the description of two clinical cases in which the sign of erection enabled the physician to make a decisive diagnosis.

PIOTROWSKI, Mansfield, O.

PATHS OF TUBERCULOUS INFECTION IN MAN. C. Y. WANG, Nat. M. J., China **10**:237-244, 1924.

Tuberculosis is extremely prevalent in China but apparently no effort has been made to find out whether of bovine or human origin. The author suggests that if any substantial percentage of Chinese patients could be found to have bovine tubercle bacilli it would open a new field of research as to the possibility of transformation of types of tubercle bacilli in the body, etc. He states that the Chinese rarely consume cow's fresh milk and practically never take it unboiled.

OPERATIVE TREATMENT FOR TUBERCULOSIS OF THE CERVICAL LYMPH GLANDS. J. S. CHU, Nat. M. J., China **10**:245-247, 1924.

The author reports excellent results from operative treatment of cervical tuberculous glands, and gives the disadvantages of tuberculin treatment of these cases. The operation is simple and the chance of permanent cure during the early stage is good. He describes the operative technic for the advanced stage. The disease in the late stage is difficult to treat but is not incurable. He believes one to two hours daily exposure to sunshine is very efficacious after operation if combined with nourishing food, fresh air and tonics.

TUBERCULOUS STRICTURE OF THE RECTUM. J. W. H. CHUN, Nat. M. J., China **11**:23, 1925.

A child, aged 4 years, was brought to the hospital complaining of difficulty in passing stools. A stricture admitting only a probe was seen 1 inch above the anus. On operation an annular mass was discovered and removed and the child made a good recovery. The pathologist who examined sections made from the mass found tubercles in all stages of development, some new, others caseous and regular giant systems were also numerous. "Stained by Ehrlich's method, isolated tubercle bacilli were seen in the periphery of caseating areas."

LUCAS, San Francisco.

Internal Diseases

CERTAIN TYPES OF CONGENITAL HEART DISEASE INTERPRETED AS INTRACARDIAC, ARTERIOVENOUS AND VENOARTERIAL FISTULAE. I. PATENT DUCTIS ARTERIOSUS. EMILE HOLMAN, Bull. Johns Hopkins Hosp. **36**:61, 1925.

Patent ductus arteriosus may be considered as an arteriovenous or a venoarterial fistula, resulting in an abnormal routing of a part of the circulating blood.

Theoretically, the flow through the ductus may proceed from the pulmonary artery into the aorta, or from the aorta into the pulmonary artery. In the first instance the lungs and the left side of the heart are avoided by the short-circuited blood, as in the fetal circulation. In the second instance, the right side of the heart and systemic circulation receive less blood than the left side and the pulmonary circulation.

In the first type a larger volume of blood flows through the right side than through the left side of the heart. From a physiologic point of view, this half of the heart should develop more fully than the left, this development being a response to the increased flow of blood through this part of the heart. This increased flow requires increased effort, and hypertrophy will inevitably result if the increased flow is large and if it is permanently maintained. In the second type the larger volume of blood flows through the left side of the heart, and hypertrophy and dilatation would be expected to be limited to this half.

Twenty-eight cases of patent ductus were studied from abstracts, with the foregoing conception as the basis for classification. The cases studied were uncomplicated by other congenital anomalies, such as a patent foramen ovale, defective interventricular septum, pulmonary stenosis, atresia of the aorta, or valvular defects. The changes found may, therefore, be ascribed solely to the presence of the patent ductus.

In sixteen cases the evidence indicates that the flow occurred from the pulmonary artery to the aorta, and these cases are classified as Type 1. In this group, the right side of the heart showed an abnormal development, in most instances equal to, and in several cases in excess of, the left side of the heart. A dilated tricuspid ring, a dilated pulmonary artery and a dilated aorta beyond the entrance of the patent ductus were recorded as characteristic of this group.

In nine cases the evidence indicates that the flow of blood occurred from aorta to pulmonary artery, and these are classified as Type 2. These cases showed a preponderate hypertrophy of the left side of the heart with a dilated aorta to the point at which the ductus was given off.

Three cases are also cited in which there were no cardiac changes. Their absence may be attributed to the narrowness of the canal, which permitted only a small volume of blood to be deflected through the opening.

The evidence furnished by these clinical observations indicates that the heart and large vessels will accommodate themselves to an increased flow through them, both by dilatation and by hypertrophy, the hypertrophy of the heart being a response to the increased effort necessary to advance an increased flow through its chambers per unit of time. The degree of hypertrophy and dilatation, we may assume, is commensurate with the volume of increased flow, and is limited to that half of the heart through which the greater flow passes, the right side undergoing a greater development than the left when the blood flows from the pulmonary artery into the aorta, and the left side of the heart

developing more than the right side when the blood flows from the aorta to the pulmonary artery.

Those cases in which a well marked cyanosis was exhibited in their clinical course fell into Group 1. In this type the ductus acts as a venoarterial fistula, the lungs are short circuited and a considerable quantity of blood escapes into the systemic circulation without aeration. Cyanosis is the logical result. Most of the cases without cyanosis fell into Group 2. In this group the systemic circulation is avoided by a part of the circulating blood, but the entire volume of each cardiac cycle is subjected to aeration. No cyanosis would be expected, and it but rarely occurs except as a terminal event.

The three cases of idiocy associated with this congenital cardiac defect fell into Group 2, in which, so it is assumed, there is an interference with the proper development of the brain, probably through malnutrition, which may be explained by the deflection of the main stream of circulating blood from the systemic to the pulmonary circuit.

NOTES ON ACUTE RHEUMATIC DISEASE OF THE HEART. WILLIAM S. THAYER, Bull. Johns Hopkins Hosp. **36**:99, 1925.

This is an analysis of twenty-five cases of acute or subacute endocarditis coming to necropsy, which appeared to be of indisputably pure rheumatic origin without demonstrable complicating bacterial septicemia.

The sequence of the disease on acute tonsillar or nasopharyngeal infections was striking.

The onset was often associated with outspoken acute articular rheumatism or with chorea.

In patients in which the arthritis or the nervous symptoms were slight, in the absence of an obvious pericarditis, cardiac involvement was revealed often only by unaccountable or persistent fever and a pronounced leukocytosis.

The earlier symptoms of acute rheumatic heart conditions were not caused by the endocarditis which, at this stage, was a mere incident of the disease. Mitral insufficiency in the early stages of an acute rheumatic heart disease is probably in most instances dependent on muscular relaxation due to myocardial changes, the earlier endocarditic lesions being usually incapable of producing a murmur. Only later, with convalescence and scarring, are the endocardial changes sufficient to produce essential valvular insufficiencies or stenoses.

The character of the fever in acute rheumatic heart disease varied greatly. In some cases it was high and continued, in others it was insignificant, remittent or intermittent.

Embolic phenomena were absent.

Albuminuria was the rule, but red blood corpuscles in the urinary sediment, so commonly found in subacute bacterial endocarditis, were not observed in rheumatic heart disease.

The fatal issue depended, in all cases, on myocardial insufficiency, although associated terminal pneumonia was not uncommon.

These twenty-five cases of rheumatic heart disease were, almost always, a true pancarditis. Endocarditis, myocarditis and pericarditis occurred with almost equal frequency.

The one characteristic lesion appeared to be the perivascular Aschoff bodies, which were found not only in the heart muscle but in the affected pericardium, in the auricular wall and even, on occasions, in the affected valves. The almost universal presence of Aschoff bodies in this series is striking.

The myocardial and pericardial changes appeared to be the gravest features of acute rheumatic heart disease and led, of themselves, to a fatal issue while the endocarditis was yet in its infancy.

The endocarditis affected the mitral and aortic valves in an overwhelming majority of cases, especially the former; but the tricuspid valve was implicated in 44 per cent.

The anatomic character of the endocarditis, the small verruscosities on the free edges of the valves and along the lines of contact need not be emphasized.

Mural endocarditis occurring in the left auricle was not infrequent. This was met with as patches, which in their acute stages were covered by a delicate layer of fibrin or by actual verrucosities; later they were represented by opaque, wrinkled, scarred-looking areas. During the acute stages these were found to overlie foci of cellular infiltration in the auricular wall, containing numerous Aschoff bodies.

STUDIES IN SCARLET FEVER. II. STUDIES ON THE USE OF CONVALESCENT SCARLET FEVER SERUM AND DOCHEZ' SCARLATINAL ANTISTREPTOCOCCIC SERUM FOR THE TREATMENT OF SCARLET FEVER. KONRAD E. BIRKHAUG, Bull. Johns Hopkins Hosp. **36**:134, 1925.

In the study of thirty-seven cases of scarlet fever treated by intramuscular injections of from 15 to 85 c.c. of serum from convalescent cases of scarlet fever, it was found that:

1. Convalescent scarlet fever serum causes a rapid improvement in the general symptoms and a slight fall in temperature and pulse rate, but produces no effect on the general rash, and does not shorten the convalescence or reduce the incidence of septic complications during convalescence.

2. A comparative study of thirty-one cases of scarlet fever showed that the intramuscular injection of Dochez' scarlatinal antistreptococcic serum in amounts of 40 c.c., administered during the first three days of the disease, caused a prompt disappearance of the toxemia, a critical fall in temperature and pulse rate, prompt fading of the general exanthem, rapid reduction in leukocytosis and rapid disappearance of the glandular enlargement.

3. The Schultz-Charlton rash extinction phenomenon can be obtained with samples of serum withdrawn from patients treated with Dochez' serum shortly after its injection.

4. A therapeutic dose of 40 c.c. of Dochez' serum was sufficient to bring about a clinical cure in moderately severe cases of scarlet fever.

5. The incidence of septic complications was low in the patients treated with Dochez' serum prior to the fourth day of the disease.

6. The patients presenting septic complications yielded slowly and irregularly to Dochez' serum.

LYTTLE, New York.

SUBCUTANEOUS EMPHYSEMA OF PULMONARY ORIGIN WITH SPONTANEOUS PNEUMOTHORAX IN INFANTS. CAROLINA CATTELAN, La Clin. Pediat. **6**:332-352, 1925.

Ten cases of spontaneous pneumotherax with emphysema were studied. In none of the cases did trauma play any part. Tuberculosis was demonstrable in seven cases, and three cases were complicated by whooping cough. The condition arose from parenchymatous lesions in the lungs. Interlobular emphysema was present in all cases, and the air escaped as a result of rupture

of the already distended peripheral alveoli by prolonged and severe cough and intense dyspnea. The air first invaded the mediastinum and then found its way into the subcutaneous tissues of the neck and chest wall.

In all cases the pathologic change began in the lungs and extended peripherally. It is possible, however, for the condition to originate in the pleural space and find its way to a bronchus, as sometimes occurs in purulent pleurisy, and then give rise to emphysema in the subcutaneous tissues.

JAUNDICE-ASCITES-NEPHRITIS. G. BENTIVOGLIO, La Clin. Pediat. **6**:355-378, 1925.

This syndrome was reported in a child, aged 5 years. The termination was fatal.

The necropsy findings were: interstitial hepatitis, acute diffused parenchymatous degeneration of the liver and nephritis. There was a slight perisplenitis.

ZAMBARANO, Northville, Mich.

THE DIAGNOSTIC VALUE OF THE GRIES NITRITE COLOR REACTION IN CYSTOPYELITIS. R. WILDMANN, Arch. f. Kinderh. **75**:185 (Feb. 10) 1925.

The Gries nitrite reaction is performed on freshly voided urine, and depends on decomposition of nitrates by bacteria. It is positive in all fully developed cases of pyelitis except in those due to the streptococcus and tubercle bacillus, but also in certain metabolic disorders such as athrepsia.

HEMPELMANN, St. Louis.

IODIDS IN SUBSTERNAL GOITER IN CHILDHOOD. GEZA PETEMYI, Monatschr. f. Kinderh. **30**:419, 1925.

In two cases in which substernal goiters produced such pressure symptoms as to suggest the necessity of operation, potassium iodid in doses of 25 mg. twice a day relieved all the symptoms.

GERSTLEY, Chicago.

THE SPECIFIC VISCOSITY OF THE BLOOD SERUM IN JOINT DISEASE. LEO KAUFTHEIL and ALBERT SIMO, Wien. Arch. f. inn. Med. **11**:191, 1925.

The specific viscosity of the blood serum in the normal person lies between 0.96 and 0.99.

In joint disease the specific viscosity is increased directly in proportion to the amount of destructive or pathologic tissue change and the degree of inflammatory manifestations.

The highest values are found in chronic primary polyarthritis and in tuberculous joint disease.

Only slight increase of the specific viscosity is found in secondary chronic polyarthritis and in arthritis deformans. One case of gout showed normal value.

SCHLUTZ, Minneapolis.

A CASE OF SPONTANEOUS PNEUMOTHORAX IN A CHILD TEN DAYS OLD. H. TIDESTROM, Acta Pediat. **4**:380 (Aug.) 1925.

The author reviews the entire literature on this subject since 1844. The patient reported developed pneumothorax quite suddenly at the age of 10 days. No adequate explanation was found, but the writer believes that a malformation of the pleura may have been responsible. The collapsed lung never

expanded, but the child survived and has been followed through a somewhat stormy career, involving numerous plastic operations to a period of comparative health at the age of 17 years.

APLASTIC ANEMIA — LEUKEMIA. AXEL ØWRE, Acta Pediat. **4**:401 (Aug.) 1925.

A case of leukemia is reported, which resembled aplastic anemia very closely in the early stages.

MYELOID LEUKEMIA IN INFANCY. NILS MALMBERG, Acta Pediat. **4**:410 (Aug.) 1925.

This is a detailed report of two cases of myeloid leukemia occurring in the first year of life.

HOLT, Baltimore.

AN UNUSUAL CASE OF CONGENITAL HEART MALFORMATION. C. JASTRZEBSKI and T. KOPEC, Polish Pediat. **5**:12, 1925.

The case concerned the postmortem findings in a boy, aged 12 years, who died of pulmonary tuberculosis and congenital heart malformation. The heart presented, besides a complete development of the intra-auricular closure, a persistence of common auricular ventricular orifice, and two common auricular ventricular valves. Of some interest is the coexistence of congenital heart malformation with advanced pulmonary tuberculosis.

PIOTROWSKI, Mansfield, O.

A GLIMPSE INTO THE QUESTION OF SPLENOMEGALY. J. T. TAI, Nat. M. J., China **11**:75-84, 1925.

During the last four years, Tai collected forty-six cases of splenomegaly among males, ranging in age from 9 to 54 years, in Yangchow Baptist Hospital. He reviews the function of the spleen, causes of splenic enlargement (infectious fevers and toxins, parasitic such as malaria, syphilis, leishmaniasis, intestinal worms, passive congestion and idiopathic or primary splenomegaly). His cases have been analyzed as to presence or absence of ascites, symptoms or findings, age, duration of splenomegaly and ascites and blood counts. He discusses the treatment of contributing causes, and suggests that splenectomy should be more commonly performed in earlier cases when there is less operative risk and more favorable outlook.

LUCAS, San Francisco.

Nervous Diseases

THE APHASIAS OF CHILDHOOD: CONGENITAL WORD-BLINDNESS AND WORD-DEAFNESS AS CAUSES OF MENTAL RETARDATION AND DEVIATION. E. BOSWORTH MCCREADY, South. M. J. **18**:635, 1925.

The author concludes that isolated defects and disabilities of varying degree in the zone of language are a frequent cause of interference with the educational progress of the individual and of undesirable affective states leading to serious temperamental, character and behavior difficulties.

In some instances the defect may be so extreme in degree and in its results as to lead to the conviction that the person is markedly defective in general intelligence, unless a careful analysis is made.

Normal and even superior intelligence is not incompatible with marked language difficulties.

Knowledge of the occurrence, prevalence and importance of aphasic conditions in children should prevail more extensively among those coming in contact with children during their early school years in order that these cases may be differentiated from those actually defective in intelligence and that the proper remedial measures may be applied.

SCHLUTZ, Minneapolis.

A CASE OF SALAAM TIC. HANS KNAUER, Monatschr. f. Kinderh. **30**:428, 1925.

In the case reported, the Wassermann reaction was positive, but in spite of intensive antisyphilitic treatmcnt the condition was not improved. The author calls attention to the relation possibly existing between the two conditions.

THE FACIAL PHENOMENON IN OLDER CHILDREN AT THE SEASHORE. WALTER FALK, Monatschr. f. Kinderh. **30**:434, 1925.

In older children sent to the seashore for convalescence from various diseases the facial phenomenon was present in a large percentage of the cases. It was more frequent in boys than in girls. After nine weeks at the seashore it had largely disappeared, to reappear again after from two to three months in the city. It diminishes in frequency from spring to fall.

GERSTLEY, Chicago.

ON THE DIAGNOSTIC APPLICATION OF THE SUGAR CONTENT OF THE SPINAL FLUID. CARL JULIUS MUNCH-PETERSON, Ugesk. f. Læger **34**:739, 1925.

The sugar content of the spinal fluid is reduced in acute meningitis just as it is in tuberculous meningitis. Chronic and purulent meningitis may show a total absence, while in encephalitis lethargica the sugar content is normal or increased.

The normal average sugar value of the spinal fluid is from 0.045 to 0.065. If the sugar content of the spinal fluid is above this normal, a blood sugar determination should be made to rule out hyperglycemia.

SCHLUTZ, Minneapolis.

EPIDEMIC ENCEPHALITIS IN CHILDHOOD. HARVEY NAI-LEE ZEE, Nat. M. J., China **10**:205, 1924.

No new material is included in this article, but a fairly comprehensive review of the subject is attempted. The author discusses the subject under such headings as general and historical introduction, epidemiology, etiology, symptomatology, incubation period, modes of onset and prodromata, disturbances of the nervous system, both as to general and localizing nervous symptoms, reflexes and signs, course of the disease, gross pathology, histopathology, clinical pathology, diagnosis, prognosis prophylaxis and treatment, during the acute and the convalescent stage. A very complete bibliography is also appended.

THE PROBLEM OF THE TREATMENT OF SPASTIC PARALYSIS: AN EXPERIMENTAL AND CLINICAL STUDY. NORMAN D. ROYLE, Brain **47**:275-292, 1924.

Royle suggests a solution of the problem of treatment of spastic paralysis. From review of the work of Boeke, de Boer, Kuno, etc., it is clear that the function of sympathetic fibers going to voluntary muscles is not definitely

known. The author experimented to determine the function of the sympathetic fibers and the relationship of function to the phenomena of spastic paralysis. His research was directed to finding a method of dealing with rigidity in spastic paralysis. Most of experimental work was done on goats because they have a definite sympathetic trunk. The results were so marked and consistent in the experimental work that he considered it justifiable to test the therapeutic value on human subjects. Sympathetic ramisectomy was done on two men in whom spastic paralysis was present in its worst form. The results were such that the author believes "procedure should be effective in practically all cases of spastic paraplegia and hemiplegia." He suggests a modification of this procedure for spastic paralysis of the lower limb; he states it is unnecessary to remove the white ramus from the second lumbar nerve in attacking rigidity in the lower limb only.

A later communication from Royle reports "sympathetic ramisectomy" done on some sixty patients. The author states that "we cannot expect a return of function when the corticospinal paths are obliterated. In patients suffering with the paraplegias and hemiplegias of infancy, when the lesion is more or less confined to the cortex, excellent results are obtained. And the same applies to traumatic lesions of the cortex."

THE EXPERIMENTAL PRODUCTION OF RIGIDITY, OF ABNORMAL INVOLUNTARY MOVEMENTS AND OF ABNORMAL STATES OF CONSCIOUSNESS IN MAN. JOSHUA ROSETT, Brain **47**:293-336, 1924.

Rosett reports strikingly abnormal neuro-muscular phenomena resulting from voluntary deep breathing. His opinion is based on more than a thousand experiments. He believes this may be utilized for physiologic study, and for the purposes of diagnosis and localization of abnormalities of the central nervous system. He reviews the main facts of blood chemistry in tetany, the general differences between manifestations of tetany in normal and abnormal persons and the action of pain in accentuating tetanic manifestations. His experiments which he considers harmless if performed carefully, are described in detail. The most striking action of hyperpnea on the cerebral cortex is as inferred from release of muscle tonus, plastic character of the rigid muscles, an over-response to affective stimuli, a diminution of power to discriminate between the finer grades of stimuli, a weakened faculty of attention, the occurrence of mental states amounting to acute dementia and of complete unconsciousness.

He states that experiments showed "that the state of attention, which is inseparable from the exercise of voluntary hyperpnea, is of itself productive of the same order of neuromuscular phenomena as that which is brought about by the induced alkalosis of the blood." Whether the "psychic" state of attention is based on a chemical change in the blood similar to that of the tetanic state is still a moot question.

THE CALCIUM CONTENT OF THE CEREBROSPINAL FLUID. MACDONALD CRITCHLEY and ELIZABETH O'FLYNN, Brain **47**:337-344, 1924.

The authors examined over 115 specimens of cerebrospinal fluid from patients suffering from chronic neurologic disorders for the purpose of determining the average figure, and "to note wherever any constant variations occur under particular pathologic or physiologic conditions." Patients ranged in age from infancy to 70 years. They found a normal calcium content of 6.2 mg. per

hundred, a constant figure apparently independent of sex or age of the patient. No diminution was found except in tetany when there was a marked fall in the lime content during the acute phase, and a more rapid rise of calcium during convalescence than is found in blood. Calcium in cerebrospinal fluid is independent of intracranial pressure, of cell and protein content, and of the Lange and the Wassermann reactions. The authors state that "examination of the calcium of the cerebrospinal fluid offers no assistance in the diagnosis of neurologic disorders."

ENCEPHALITIS PERIAXIALIS DIFFUSA. L. BOUMAN, Brain **47**:453-488, 1924.

Two cases of encephalitis periaxialis diffusa, a very characteristic structural disease first reported by Schilder in 1912, are analyzed. This is a disease rarely seen and clinical diagnosis can usually only be made on necropsy. In Bouman's cases there was destruction of the white matter of both hemispheres; the fibrae arcutae, that is, the subcortical fibers, remaining unaffected. The literature of the disease and the reported cases are reviewed at length. The author also gives a very comprehensive table which contains the names of all the reported cases, sex, age, duration of illness, general and psychical symptoms, disorders of vision, optic disks, ocular movements, pupils, disorders of speech, paralyses, contractures and tremors, tendon, plantar and abdominal reflexes, sensation, epileptic attacks and spasms, Wassermann in serum and cerebrospinal fluid tests, and globulin, cell increase and pressure in cerebrospinal fluid. The duration of the illness in twenty-one cases was under two years, but in four cases it was longer and the ages of the patients ranged from 1 to 43 years.

THE ENCEPHALITIS PERIAXIALIS OF SCHILDER. JAMES COLLIER and J. G. GREENFIELD, Brain **47**:489-519, 1924.

The authors report two cases of encephalitis periaxialis, one of which occurred in 1902, ten years before the appearance of Schilder's monograph. A study of the recorded cases leads these authors to believe that the clinical aspect of the disease is so nearly identical in all the cases that it is possible to set down a clinical description which should aid in the recognition of future cases. They describe it as "a malady usually occurring in children and young subjects with no tangible causal factors or antecedents. The onset is a few days, the course progressive with some remissions to a fatal issue, the duration from a few months to three years. The chief early sign is cerebral blindness which becomes complete, to which is added mental reduction and increasing spastic paralysis. Unsteadiness from parietal involvement and deafness from temporal involvement may be conspicuous. The amentia increases and passes into coma which terminates the illness. The condition, usually bilateral, may commence on one side or may be confined to one side." They believe the pathologic picture is a good explanation of the symptomatology. The article includes short analyses of the recorded cases. Description of the morbid anatomy and symptoms are considered in detail. Numerous illustrations are included. Any physician having a case of suspected encephalitis periaxialis would do well to read the two careful studies of this malady in this issue of *Brain*, the one by Bouman and this one by Collier and Greenfield.

A Study of the Lipoids in Neuronic Degeneration and in Amaurotic Family Idiocy. E. Weston Hurst, Brain **48**:1-42, 1925.

A review of the literature showed recognition by many observers of the presence in degenerative conditions of such bodies as the neutral fats, fatty acids, cholesterin, cholesterin esters, phosphatids and cerebrosids. The purpose of this study was to determine the nature, mode of production and time relation of various products of nervous disintegration and to compare results obtained by various staining methods on the seven cases studied to ascertain their value. Tissues of the brain and cord were examined for fatty substances, being cut by the freezing microtome and stained by several different methods: Scharlach red in three different ways, osmic acid before and after the action of potassium bichromate, the Nile blue method of Lorrain Smith, the Klotz method for staining fatty acids, the Kultschitsky-Pal method for myelin, neutral red, and unstained sections were examined for colored pigments and with polarized light for doubly-refracting lipoids, and tissue was also passed through celloidin and the sections stained by general and special tissue stains.

Of the three cases of tract degeneration studied at different periods after the initial lesion only one occurred in a child. This boy suffered from ulcerative endocarditis resulting in a cerebral embolism which caused hemiplegia. Two cases of amaurotic family idiocy and one of cerebromacular degeneration were also studied.

Hurst states that in cell protoplasm no lipoid is detectable with fat stains in the normal condition, and if present is either in a chemical combination with protein or in a finely divided condition in an emulsion. He concludes that phosphatids and cerebrosids found in cases of neuronic degeneration have been liberated from a chemical combination with some other cellular substance, and as they unite readily with protein, it may be assumed that they exist in the form of lipoproteins.

Respiratory Disorders in Epidemic Encephalitis. W. Alden Turner and Macdonald Critchley, Brain **48**:72-104, 1925.

This article consists of a careful review of the literature on respiratory disorders following epidemic encephalitis and a detailed discussion of seven illustrative cases. The authors classify the respiratory disorders as follows:

1. Disorders of the respiratory rate.
2. Dysrhythmias, or disorders of the respiratory rhythm.
3. Respiratory tics.

Any combination of these symptoms is possible in a given case. Turner and Critchley believe that these clinical manifestations cannot be considered as accidental or "hysterical" phenomena, "but that they constitute a very definite clinical entity playing an important rôle in the symptomatology of the disease." Their conclusion after a review of the theories of pathogenesis, bulbar, thalamic and peripheral, is that this "lies in a derangement of the involuntary psychomotor control of respiration, which is maintained by various corticopontine pathways, capable of anatomic demonstration. The lesion, therefore, is placed at a level higher than the so-called respiratory 'centres.'"

Prognosis is serious when these disorders appear during the acute phase, when they appear as sequelae the outcome is questionable. No known treatment was found to be of any advantage.

A Clinical Study of Increased Intracranial Pressure in Sixty Cases of Cerebral Tumor. W. Russell Brain, Brain **48**:105-125, 1925.

This is an analysis of the signs and symptoms of increased intracranial pressure in cerebral tumors, which term includes neoplasms and certain localized infective conditions resulting in increased intracranial pressure. Brain divides his cases into three groups: (1) twenty-four cases in which the precise situation and extent of the tumor were ascertained at necropsy; (2) fourteen cases in which the site was verified by operation but no necropsy; (3) twenty-two cases with no necropsy and operation if performed gave no reliable information as to site.

Focal signs in some cases were too slight or conflicting for accurate and early localization. In only 60 per cent. of the cases were the three classical symptoms present together. Headache was present in 88 per cent. of cases, papilledema in 75 per cent. and vomiting in 65 per cent. Headache is of little value in localization unless confined to or predominating on one side. Two types of headache were significant: (1) pain in the occipital region on one side and radiating through the bases of the mastoid process to the frontal region on the same side, when they were usually due to a tumor in the posterior fossa on that side; and (2) pain arising in the occipital region and radiating over the vertex to the brow when suggestive of onset of internal hydrocephalus.

The time of onset of vomiting in relation to that of papilledema is more reliable in localization. The fact that vomiting is invariably a symptom of hydrocephalus explains the relationship between its time of onset and the site of the tumor.

Tumors of third and fourth ventricles, of the cerebellum, and one case of occipital tumor in Brain's Group 1; tumors of frontal, parietal and temporosphenoidal lobes in Group 2. Vomiting coincided with the onset of illness and was one of the first complaints in all cases in Group 1. Vomiting occurred in only a quarter of the cases of Group 2 during the early stage of the illness and was entirely absent in half of the cases. In Group 1 and in tumors of the pons, papilledema was due to hydrocephalus; in Group 2 to local rise in intracranial pressure from a tumor. Vomiting preceded papilledema in Group 1, and was apparently an earlier sign of hydrocephalus. In Group 2 papilledema preceded vomiting, since with tumors of the frontal, parietal and temporosphenoidal lobes the rise in intracranial pressure usually causes a rise in pressure within the optic sheaths earlier than it leads to obstruction of the aqueduct of Sylvius.

The Histology of Juvenile Amaurotic Idiocy. J. G. Greenfield and Gordon Holmes, Brain **48**:183-217, 1925.

This is a very extensive record of two cases of juvenile amaurotic idiocy belonging to the same generation of a family of pure English stock. The authors believe there is a close connection between these cases and the Tay-Sach's form, even though they are not confined to the Jewish race, appear later in life, progress more slowly and the blindness is not associated with the same ophthalmoscopic picture. They cite the observations of Batten, Vogt and others establishing a juvenile type of amaurotic idiocy.

Both of the authors' patients showed the first signs of disease at the ninth year, the first one dying five years later, the other being sent to an institution. They give a very detailed account of the pathologic examination of the first

patient, with illustrations. They state that it is unnecessary to emphasize resemblance of histologic lesions and clinical aspects of this disease to those of infantile type though there are obvious differences also. They suggest the division of recorded cases of juvenile amaurotic idiocy into two groups, one in which the cerebellum had undergone general atrophy and is more severely affected than the rest of the brain, the elements of the granular layer and the afferent cortical fibers being especially involved; in the other group, the cerebellum only is affected to the same degree as the rest of the nervous system. They define retinal changes "as a primary change in the ganglion cells, combined with an independent degeneration of the outer neuronic elements of the retina, which in some cases extends to the inner nuclear and inner reticular layers." The affection of the outer layers differentiates the retinal lesions of the juvenile from those of the infantile type of family amaurotic idiocy.

A Clinical Study of Sensory Jacksonian Fits. Otto Sittig, Brain **48**: 233-254, 1925.

The author discusses the methods of Hughlings Jackson and Arnold Pick. Sensory jacksonian fits he groups into classes according to the manner paraesthesia spreads. In his first class are the cases "in which the sequence of the parts of the body affected by paraesthesia corresponds strictly to arrangement of the sensory points in the postcentral gyrus." In class two, paraesthesia spread over the whole half of the body and the sequence is not in the order of cortical points. In class three, paraesthesia may correspond to an axial type, and spread either along the radial or ulnar part of the arm or the anterior or posterior side of the leg or may descend on one side and ascend on the other. He describes other cases in which "sensory fits" followed other functional patterns. He accepts the views of Jackson, Sherrington and Head that spread of paraesthesia depends on the strength of the stimuli. If the stimulus is weak the paraesthesias do not spread widely and may correspond with the order of the sensory points in the postcentral gyrus. "If the excitation extends it follows certain functional patterns, which must not be regarded as preordained centers and pathways. Such functional patterns are for instance, the tips of the fingers, the corner of the mouth, the thumb and the big toe, Head's 'schema' of the body, and finally, the preaxial and postaxial types. The latter may depend on ontogenetic factors."

The Pathogenesis of Subacute Combined Degeneration of the Spinal Cord with Special Reference to Its Connection with Addison's (Pernicious) Anemia, Achlorhydria and Intestinal Infection. Arthur F. Hirst, Brain **48**:218-232, 1925.

This is a discussion of subacute combined degeneration and Addison's anemia to oral sepsis associated with absence of free hydrochloric acid throughout the digestion with resulting intestinal infection and toxemia. The author believes the division between subacute combined degeneration of the cord and Addison's disease to be purely artificial. Complete achlorhydria is present in practically all patients with Addison's anemia and in all with subcute combined degeneration to whom test meals were given or gastric contents were examined. "Achlorhydria generally due to constitutional achylia, an inborn error of functional activity independent of anatomic changes in the mucous membrane." It is probably familial, which would explain familial occurrence of Addison's anemia, though there are few opportunities of proving this. The author cites

Weinberg's family in which the father with Addison's anemia had four healthy children, three of whom like the father had complete achylia gastrica.

The author discusses the danger of oral sepsis from teeth or tongue in the absence of the germicidal barrier formed by the free hydrochloric acid of the gastric juice, intestinal toxins and the blood picture in Addison's anemia, and the anemia associated with subacute combined degeneration.

Prophylaxis in patients showing achlorhydria should consist of taking hydrochloric acid for the rest of their life and the eradication of oral sepsis. Since this is a familial condition the gastric contents of all members of the family of the patient should be examined, and if achylia is found, the same precautions should be taken. Prevention of Addison's anemia and subacute combined degeneration of the cord depend on early diagnosis and treatment. Treatment should consist of removal of the teeth, vaccine, administration of hydrochloric acid, culture of *B. acidophilus* and powdered animal charcoal.

HEMANGIOMA OF THE PIA MATER CAUSING COMPRESSION PARAPLEGIA. PERCY SARGENT, Brain **48**:259-267, 1925.

"More or less localized mass of blood-vessels, nevoid in character, lying between pia and the arachnoid" may give rise to symptoms resembling those of spinal tumor. These were first noted by Gaupp in 1887. Among cases reported by Stanley Cobb was one of a boy, aged 8 years, whose first symptom was a sudden sharp pain in the back which disappeared in four days. There was another attack three days later, which was more intense with numbness in the left foot. The latter symptom spread up the left leg and down the right. On examination, there was a complete flaccid paralysis with loss of reflexes and anesthesia up to the umbilicus. Two months later the tendon reflex returned with a positive Babinski sign. Laminectomy was performed from the sixth to the tenth thoracic vertebrae, which showed a tangle of large vessels overlying a flattened cord. No ligation was done and the dura was left open. There was no relief. There was a large nevus of the skin over the right lower ribs behind, and three other smaller nevi were at the same level. In most of the recorded cases and the author's four, the vascular mass consisted of dilated tortuous veins only, almost constituting a venous angioma. The author states that these venous angiomas resemble congenital nevi found elsewhere in the body and are perhaps of the same nature. There is nothing to assist the differential diagnosis as to age, sex or segmental level. The most striking feature in many of the recorded cases was variation of symptoms from time to time, also more or less complete recovery between "attacks." The value of operative interference is very doubtful.

LUCAS, San Francisco.

Diseases of the Eye

REPORT OF A CASE OF ORBITAL NEURINOMA. MARTIN COHEN, Arch. Ophth. **54**:426, 1925.

A boy, aged 11, presented a proptosis of the right eye without failure of vision, despite a choked disk of seven diopters. A general physical examination including Wassermann and tuberculin tests and the roentgen ray were negative. A Krönlein operation revealed a soft mass in the orbit extending from below the globe along the outer side of the optic nerve to the apex of the orbit. It was removed by blunt dissection, except where it was attached to optic nerve sheath at the apex of the orbit, where it was severed with scissors. Following the operation the eye turned in, as a result of traumatic

paralysis of the external rectus, and vision was entirely lost because of the secondary optic atrophy.

Microscopic examination revealed a thin capsule, large blood vessels throughout the tumor, hemorrhages beneath the capsule and fibers extending from the latter into the tumor. Elongated spindle cells with various sized and shaped nuclei together with dilated lymph spaces made up the body of the tumor.

The diagnosis was neurinoma (neurofibroma) of the posterior ciliary nerve.

A Case of Neurofibromatosis with Buphthalmus. Alfred Wiener, Arch. Ophth. **54**:481, 1925.

A boy, aged 2 years, presented a buphthalmus of the left eye, with a neurofibromatosis of the fifth nerve involving lids, jaw and forehead on one side. A general examination was otherwise normal, except that the left orbit was enlarged. The left eye was removed and showed the typical microscopic changes of buphthalmus. A mass removed from the forehead showed the characteristic picture of Recklinghausen's disease. Since 1897, many authors have reported cases illustrating the association of buphthalmus and neurofibromatosis.

Wescott, Chicago.

Diseases of the Skin

Sweating and Sudaminal Eruptions in Infancy. A. B. Marfan, La Clin. Pediat. **6**:321-331, 1925.

To prevent the occurrence of the various skin eruptions associated with excessive sweating, therapeutic measures directed toward the suppression of sweating are the only really successful means we have. In spite of rigorous bathing with antiseptic soaps and the use of sterilized linen, the pustules, bullae and abscesses continue to form. Vaccinotherapy has proved ineffectual. The author has outlined the following procedures in his course of treatment:

1. Avoid excessive coverings; e. g., clothing, blankets, etc.
2. Do not keep the infant in a too warm atmosphere.
3. Breast feeding is to be encouraged as much as possible.
4. Combat vigorously any tendency toward rickets, since this disease is a common predisposing factor, if not the exciting cause, of excessive sweating and chronic pyodermatitis. To treat rickets successfully the author recommends the following methods: (*a*) epinephrin with calcium phosphate, (*b*) cod liver oil and (*c*) ultraviolet ray. To determine which of these methods is best for the given case, a trial of each or all of them is necessary.

Zambarano, Northville, Mich.

Eczema of Infants. Kaj Baagøe, Ugesk. f. Læger **35**:760, 1925.

This paper presents a comparison of the ideas and facts held by German and American investigators in reference to eczema of infants. The German investigators place eczema of infancy and early childhood in the category of exudative diathesis, while the Americans believe eczema to be an allergic manifestation. No attempt is made to decide how eczema should be classified, although the author appears to favor the American view.

The author discusses the following interesting facts and ideas. 1. Eczema of early childhood is of two kinds, one that shows positive cutaneous reac-

tions and one that does not. 2. There is a concomitant eosinophilia which may be due to the same irritant as that causing the eczema or a result of the skin involvement. 3. The presence of specific antigens for fats is still in doubt. 4. The skin of fat children is less resistant to irritants. 5. The appearance in the mother's milk of substances which sensitize the child to certain foods, such as egg albumin, barley and oatmeal, still requires, according to the author, further investigation.

The most successful treatment of eczema in infancy and early childhood is to keep the child in good mineral metabolism and only moderately well nourished. This is done by reducing the carbohydrates and more particularly the fat content of artificial foods.

SCHLUTZ, Minneapolis.

Surgery and Orthopedics

INTESTINAL OBSTRUCTION IN AN INFANT DUE TO MESENTERIC CYST WITH VOLVULUS. G. D. CUTLER and J. C. MERRIAM, Boston M. & S. J. **193**:550 (Sept. 17) 1925.

This is interesting because of the rarity of mesenteric cysts in infancy. They usually do not become large enough to cause symptoms until after the fourth year. A boy, aged 3½ months, breast fed, was admitted to the children's hospital in a state of profound shock, with a history of vomiting for two days and disinclination to nurse. The temperature was 97 F., the pulse 160 and poor quality and the respirations 60. The abdomen was distended, fairly rigid and apparently tender, with shifting dulness in the flanks. The rectal examination was negative. The operation under ether anesthesia revealed cloudy, foul smelling fluid; most of small intestine was plum colored and the peritoneal coat was lusterless; there was a tense mesenteric cyst, about the size of a goose egg, about 24 inches below the duodenum; there were complete volvulus of the mesentery, thrombosis of the mesenteric blood vessels, and gangrene of the gastro-intestinal tract from the duodenum to the rectum. The volvulus was untwisted, but no attempt was made to remove the cyst. The patient died one hour after operation. References are given to other reported cases.

GENGENBACH, Denver.

Miscellaneous

MASTITIS OF THE PUEPERIUM CURED WITH CAMPHOR. G. ALLARIA, La Prat. Pediat. **2**:33-36, 1925.

A young primipara developed a severe mastitis incident to fissured nipples, on the twenty-third day following delivery. The abscess ruptured spontaneously after twenty-five days of fever. The temperature dropped to normal, but the profuse discharge from the breast continued, resulting in the development of a fistula. A diagnosis of subacute fistulous mastitis with galactorrhea was made when seen by the author (2½ months from onset). He started daily injections (hypodermically) of camphorated oil (from 10 to 20 per cent.). Within a week the discharge stopped, and within ten days the fistula healed.

The rapidly spreading mastitis evidently attacked the functioning glandular structure, and, in the milk, found an excellent culture medium for further propagation of the bacteria.

AUTOVACCINOTHERAPY IN CHILDREN. L. BUONACORSI, La Prat. Pediat. **2**:95, 1925.

The author urges autovaccinotherapy in infants and in children. He believes that autogenous vaccines are far superior to the ordinary stock preparations,

because once an organism invades the body it becomes biologically different from the laboratory culture. He makes the following report of cases treated with autogenous vaccines. Good results are claimed for all cases excepting the pleural empyemas, in which a combination of surgery and vaccine proved more efficacious.

Thirty-four cases of gonorrheal vulvovaginitis, the ages ranging from 20 days to 11 years.

Two cases of gonorrheal arthritis, aged 28 days and 6 months respectively.

Twenty-two cases of purulent otitis, ages ranging from 10 months to 8 years.

Eighteen cases of *Staphylococcus pyodermatitis,* ages ranging from 26 days to 7 years.

Nine cases of colon bacillus cystitis, ages ranging from 2 months to 6 years.

Three cases of cerebral spinal meningitis, the ages ranging from 4 to 12 months.

One case of pneumococcus septicemia, aged 5 years.

One case of putrid pleurisy (diplococcus catarrhalis), aged 5 years.

Five cases of pleural empyema, the ages ranging from 21 months to 2 years.

ZAMBARANO, Northville, Mich.

CLINICAL EXPERIENCES WITH HEVITAN. GÖTZKY, Arch. f. Kinderh. **75**:195 (Feb. 10) 1925.

Observations were made over a period of ten months on eighty-eight infants, to whom hevitan (a yeast preparation, made according to the formula of Reyher) was administered in addition to the regular infant dietaries. The results obtained were far better than any hitherto seen with the normal feeding formulas, and seem to depend on the administration in this way of the vitamin B. Digestion, appetite and appearance were improved, and there was a good gain in weight with increase of resistance to infections. In some instances, deficiency of vitamin B was combined with lack of vitamin C, and improvement did not occur until orange or lemon juice was added to the hevitan therapy.

HEMPELMANN, St. Louis.

THE PRESENT STATUS IN THE TREATMENT OF METASYPHILIS. W. WEYGANDT, Ztschr. f. d. ges. Neurol. u. Psychiat. **96**:7 (April) 1925.

Möbius about three decades ago spoke of tabes and general paralysis metasyphilitic infections, and while he looked on the process as syphilitic, he thought that the effect probably was produced by some toxin which attacked the nervous system under certain favorable conditions. The demonstration of spirochetes by Noguchi proved the syphilitic nature of these conditions. Virchow, in 1898, however, stated that definite anatomic proof of syphilitic infections in tabes and paresis is seldom found, and the inefficiency of antisyphilitic treatment in these diseases was further demonstration of their nonsyphilitic nature.

Several theories have been brought forward to explain the occurrence of tabes and paresis: 1. One theory is that of hereditary disposition, which bases its argument on the difference in the occurrence of metasyphilitic conditions in civilized and barbarous or primitive nations. Cases of tabes and paresis, however, occur among uncivilized peoples. 2. Kraepelin propounded the theory that during the last hundred years the human constitution has changed so as to make it susceptible to the toxin which causes the metasyphilitic condi-

tions. Proof of this is found in the increased number of cases of paresis and tabes during the last century, and their infrequency before the nineteenth century. 3. Erb advanced the conception of definite neurotropic strains of spirochetes with a predilection for attacking the central nervous system. Plant and Mulzer corroborated this experimentally by finding a neurotropic strain in a dog, after several hundred transfers. Furthermore, Mulzer and Plant induced spinal fluid changes in a dog by the injection of paretic cortex. At necropsy the brain showed pictures similar to that seen in human paresis. Levaditi claims to have isolated four neurotropic strains of spirochetes. O. Fischer would differentiate a tropic strain for paresis, tabes and cerebrospinal syphilis, but Weygandt does not subscribe to this idea. The question is complicated, moreover, by the fact that there are intermediary stages between tabes and paresis just as there are between paresis and cerebral syphilis. Weygandt believes that the conception of neurotropic strains, despite the work of Plant and of Levaditi, needs confirmation. 4. Still another idea as to the origin of tabes and paresis has been advanced by Nonne, who considers these conditions as artificially produced by improper treatment. Statistics by Krou and Pilcz show that the shorter the treatment the shorter the period between the primary infection and the occurrence of tabes and paresis. Gärtner has reported a marked increase in paresis in recent years in Germany. In 178 prostitutes with positive fluid findings Kyrle found that 33 per cent. were untreated, 22 per cent. were treated with mercury, and 44 per cent. were treated insufficiently with mercury and arsenic. Experimental proof of the fact that insufficient treatment can cause these conditions in the nervous tissue is furnished by Plant, who infected a dog with a non-neurotropic strain of spirochetes, and then by insufficient treatment with arsphenamin induced positive spinal fluid findings. Weygandt himself believes that a great many patients are insufficiently treated, and that more intensive treatment will yield better results. He believes the spirochetal infection causes the production of immune bodies, and that the occurrence of skin lesions indicates the index of protectives for the internal organs, especially the nervous system. The fluid becomes infected in the secondary stages, and the spirochetes remain dormant for some time in the meninges and blood vessels only to become active later and disseminate in the nervous tissue. Lewandowsky has demonstrated that tubercle bacilli may become activated in this way. 5. Gennerich, too, has propounded a theory regarding the pathogenesis of general paresis. Briefly, his theory is that as a result of inadequate treatment the virulence of the syphilitic infection is mitigated and the body defence weakened. Hence a chronic latent syphilitic meningitis arises and produces adhesions of the pia to the cortex. In proportion to the amount of this adhesion and degeneration, there is a more or less abundant invasion of the cortical parenchyma by the cerebrospinal fluid, for one of the functions of the pia is to prevent the brain tissue from being soaked with fluid. The invasion of the cortex by the fluid causes the paretic condition. Weygandt does not believe that hypothesis has been amply proved. 6. Hauptmann believes that the hyperpermeability of the meningeal vessels permits toxic substances to enter the fluid from the blood, in this way causing infection. 7. Still others believe in a proteolytic process.

The treatment of tabes and general paresis goes far back. The middle generation of neurologists and psychiatrists are descendants of the period of therapeutic nihilism characterized by the attitude of Möbius that there is no cure for paresis. Weygandt delves far into the past and produces evidences of cures

of psychoses from Galen and Hippocrates. Nasse, in 1870, reported improvement in paresis by malaria and also variola. Hemming, 1877, described a seven year remission in paresis after typhoid. Cases of improvement and apparent cure in paresis have been reported after measles, erysipelas, variola, pneumonia, diphtheria, cholera, phlegmons, abscesses and even chorea. Weygandt reports a patient of his who had a remission of one and a half years after a phlegmon, and calls attention to remissions after influenza and typhoid fever. The various other methods of treatment are discussed, e. g., mercury, endolumbar treatments and other methods. Gennerich reports very good results by means of the endolumbar method, but Weygandt has seen no results in his paretic patients. Knauer's method of arsenic injection into the carotid has produced no marked results. Cistern treatments as advocated by Purves-Stewart and Nonne with good results have been of doubtful efficacy in the hands of the author. The same is true of cerebral injections. Numerous methods are detailed, but with no striking results. Silver arsphenamin seems to be of some value in decreasing the serologic findings. Newer arsenical and bismuth preparations are mentioned. Unspecific remedies have recently been used with some success. Besides substances such as albumose, dentero-albumose, casein, milk preparations and other substances, such as "nucleinate" preparations have been used. Donade has reported 47.6 per cent. good remissions and 24 per cent. slight remissions in twenty-one patients treated with sodium nucleinate. Tuberculin too has been used since 1900 as a means of treatment in metasyphilis. Weygandt reports remissions in one third of his cases, much more than in spontaneous remissions. Wagner-Jauregg has reported twenty-six per cent. of remissions in paretic persons treated with polyvalent staphylococcus vaccine, and since 1917 Wagner-Jauregg has used malaria for the treatment of paresis, with startling results.

Weygandt points out that the use of malaria in the treatment of paresis is attended with certain dangers. Malaria itself is likely to affect the nervous system; in the severe tropical forms one may have epileptiform convulsions, unconsciousness, spasms and local twitchings, delirium and coma. In chronic malaria one may have all kinds of neuralgia and neuritides, optic neuritis, ocular palsies and often a polyneuritis. Besides, deaths which follow immediately after or during the malaria are not uncommon. The danger of infection by contact is very real, and Weygandt states emphatically that this treatment should be confined to the hospital and not tried in private practice. Following the "cure" there often occurs an anemia of more or less severity. In one of the author's cases a pernicious anemia occurred more than six months after the malaria cure. Among several hundred cases of paresis treated with malaria by Weygandt there occurred complete remissions in 26 per cent. and satisfactory remissions in 18 per cent., the remissions being more complete and longer than spontaneous remission. In many cases there occurred an improvement in the reaction to light, and disappearance of the stiff pupil occurs, even though not common. The patellar reflexes often return and improvement in sight with optic atrophy often occurs. The serologic improvement is even better than the clinical. The pleocytosis disappears, the globulin reaction becomes weaker, and the blood Wassermann test becomes negative, usually before the fluid Wassermann test. Wagner-Jauregg considers the fluid reactions unimportant for prognostic significance. Weygandt reports on the histologic examination of brains of paretic persons treaetd by malaria. In general, he says that there is a freedom from spirochetes and a tendency of the inflammatory phenomena

to disappear, sometimes completely, just as in stationary paresis. Treatment of paresis by recurrent fever, however, has yielded satisfactory results with a fairly high mortality.

ALPERS, Philadelphia.

THE EFFECT OF ATROPIN ON INFANTS. GUSTAV LINDBERG, Acta Pediat. **4**:309 (Aug.) 1925.

The author obtains the best results with a 0.5 per cent. alcoholic solution of the drug. Great differences are found in the tolerance of individual infants for atropin. Most infants tolerate it well, and can be accustomed to large doses. In order to be effective, the drug must be given until a vasomotor reaction — flushing of the skin — follows. The author has successfully used it (1) as a sedative for neuropathic infants, (2) for eczema, (3) for habitual vomiting, and (4) in certain cases of pyloric stenosis.

HOLT, Baltimore.

Society Transactions

NORTHWEST PEDIATRIC SOCIETY

Rochester, Minn., July 18, 1925

ROOD TAYLOR, M.D., *Chairman*

INFANTILE MYXEDEMA. Presented by DR. H. F. HELMHOLZ.

The patient was brought to the Clinic because of stunted growth and inactivity. His birth weight was 7 pounds, 8 ounces. He walked when 1 year of age and talked at that time. His photograph, taken when he was 1 year old, shows him to be normal in size and appearance. At 15 months, he suddenly became very thirsty, consuming excessive amounts of water and passing large amounts of urine. A diagnosis of diabetes was made. The condition disappeared in the course of the next six months. The child was entirely free from sugar when on a liberal diet. At this time the mother noticed that he was not growing. Six months later, he was put on 0.25 grain of thyroid three times a day. The boy grew 3 inches in the next five months. At the end of that time, while under treatment, the diabetes returned. Consequently the thyroid treatment was discontinued.

At present he is on general diet. The urine is free from sugar and the blood sugar is normal. The basal metabolic rate is minus 45. It is unusual to find an insufficiency of two glands of internal secretion. There has been no history of illness to account for the conditions. The diabetes gradually disappeared as the myxedema developed, but reappeared when thyroid therapy was instituted.

DISCUSSION

DR. MYERS: We took care of this patient and there was quite a long period of time when his blood sugar was normal, although there was sugar in the urine.

DR. TAYLOR: How much thyroid extract did you give him?

DR. MYERS: One-fourth of a grain three times a day.

DR. SCHLUTZ: Does the patient have any abnormalities?

DR. HELMHOLZ: None.

DR. STEWART: What is the estimation of his mental age?

DR. HELMHOLZ: He is very slow in getting started, but he is much brighter than he appears.

DR. STEWART: Isn't that rather characteristic?

DR. HELMHOLZ: Yes, of infantile myxedema. This boy probably had a normal thyroid up to 3 years of age.

DR. TAYLOR: Has his treatment been continued until he came here?

DR. HELMHOLZ: No, he had thyroid medication from August till December, 1919; since then none. It was discontinued because of the glycosuria.

DR. MYERS: The last time he came to us he had an attack of diabetic coma, and we gave him insulin to get him free from sugar. That was since 1919.

DR. MYERS: Have you a picture of his wrist? What development does it show? My impression is that our picture showed lack of development. If this

were infantile myxedema developing during the first or second year of life, would that affect the development of the carpal centers as it would if it were cretinism of congenital origin?

DR. HELMHOLZ: If it were cretinism he would have one or possibly two centers, but as he had six or seven I feel that this is a myxedema. I think his picture is the best evidence we have that we are dealing with myxedema instead of cretinism. I do not believe that a child with thyroid insufficiency could have talked or walked at 1 year.

DR. HELMHOLZ presented a case of chronic ulcerative colitis, showing also a roentgenogram of the colon which revealed the typical absence of haustra.

DISCUSSION

DR. MYERS: What therapy are you giving in this case?

DR. HELMHOLZ: The patient just came in yesterday.

QUESTION: What diet would you give?

DR. HELMHOLZ: Dietary measures do not seem to make any difference. We expect to give a diet with little residue.

DR. ANDREWS: I have been interested in ulcerative colitis. We have had one case which I followed for some time in the hospital. The child died from hemorrhage. The etiologic factor was not found. Have you had any cases which resulted fatally from hemorrhage?

DR. HELMHOLZ: No.

DR. MYERS: Do you interfere surgically on these patients?

DR. HELMHOLZ: Only when the patients grow worse in spite of all treatment.

DR. TAYLOR: What about the use of iodin?

DR. HELMHOLZ: The results are only fair.

DR. TAYLOR: Do you give any therapeutic test with emetin, that is, after failure to find amebae?

DR. HELMHOLZ: Emetin has been used in some cases. In one patient, in spite of treatment, there was no improvement; in fact the condition became worse and we never found amebae a second time.

QUESTION: What is you favorite treatment?

DR. HELMHOLZ: The treatment that we have been using with the greatest success has been removal of foci, followed by the use of vaccine made from material taken directly from the ulcers or isolated from bloody mucus. In addition, we have given transfusions and a bland residue free diet.

DR. STEWART: Have any of your patients been tuberculous?

DR. HELMHOLZ: Tuberculosis has been excluded in all the cases of ulcerative colitis.

OBSERVATIONS ON ATROPIN REACTIONS. Presented by DR. O. GROB.

The effect of atropin was observed on the pulse, superficial vessels, pupils, salivation, and bladder pressure. In the majority of the cases there was slowing of the pulse from two to ten minutes after the injection of atropin. In the average number of cases, the pulse reached the rate it had before injection, 16 minutes after injection. After this the pulse became accelerated.

Flushing of the face occurred frequently. In a few instances there was flushing of the body. In a very few cases there was slight mydriasis. Thirst

was noted only following large doses of atropin and was not a frequent symptom. The effect on the bladder pressure was observed in eight cases. As a rule, there was a decreased tonicity. The effect of the drug varied markedly at different times on the same person, even when the dose remained the same.

DISCUSSION

DR. AMBERG: We were simply interested in getting the general effect on the slowing of the pulse. Owing to the observations made previously, naturally I was greatly interested in the effect of the drug which has been used occasionally with benefit in enuresis. This is one of the drugs which has been accused of being able to work only by suggestion. In addition to the usual effects, atropin frequently lowers the pressure of the bladder at rest. Furthermore, it has been shown recently that it exercises an influence on sleep. We have another example of the risk in ascribing the benefits of therapeutic agents solely to suggestion.

DR. TAYLOR: It seems to me that this is a very illuminating piece of work. Maybe I am drawing the wrong conclusions, but my experience with atropin is this, that you cannot tell what it is going to do. I use it in colic. Some of the time I get good results, sometimes not. When do you get the slowing of the pulse?

DR. GROB: Between two and fifteen minutes, never after fifteen minutes. In only two cases out of the twenty-four after ten minutes; the average was eight minutes.

DR. TAYLOR: How long after injection does the acceleration appear? How long does it last?

DR. GROB: Dr. Amberg's average is eighteen minutes after injection. It lasts over an hour, sometimes longer.

SPLENECTOMY IN PURPURA OF AN UNUSUAL TYPE. Presented by DR. M. M. MELSON.

Within the last year we have seen two unusual cases of purpura hemorrhagica that have improved, at least temporarily, following splenectomy.

The first patient, D. A., was a girl, aged 8 years, who had had recurring epistaxis since the age of 14 months, bleeding from four to twenty times each year, and showing large discolored areas when bruised. During her three months hospitalization here she had nine intramuscular injections of whole blood and seven transfusions without noticeable improvement. Splenectomy was performed August, 1924. Before splenectomy there was nonretractility of clot; after operation retractility occurred within twenty-four hours. Bleeding time continued to be more than one hour and the platelets were around 300,000. Since the operation the patient has had but one attack of epistaxis which was caused by a severe blow in December, 1924, and which stopped immediately on packing. Previous to removal of the spleen, it had required a doctor to control the bleeding and the longest period free from hemorrhage had been nine months.

The second patient, P. M., a girl, aged 4 years, entered the Clinic in May, 1925. One week before entrance the mother had noticed hemorrhagic spots on the body surface. On examination, the child showed marked gingivitis. There were many subcutaneous hemorrhages on the arms and legs and a few on the back and abdomen. The bleeding, coagulation, and prothrombin times were prolonged. The patient was hospitalized. At entrance, the platelet count was 98,000, but in about two weeks it had dropped to 56,000. Three trans-

fusions were given before splenectomy was performed. The platelets rose to 208,000, but have dropped to 130,000 at the present count. The general condition is much improved.

ACUTE CHANGES IN THE KIDNEY AND URETER FOLLOWING TYING OF THE URETER. Presented by DR. HELMHOLZ.

This study was undertaken in an attempt to discover what acute changes would take place in the kidney and ureter after an obstruction of the ureter without an infection.

As early as three hours after tying the ureter, there may be clots of blood in the nephrotic sac. After four hours changes begin to appear in the walls of the kidney pelvis. After the clots appear, it is only a short time before definite hemorrhages in the parenchyma are apparent.

After eight hours the peripelvic tissues show very definite hemorrhages, and collections of leukocytes appear in the vessels of the pelvis. After eighteen hours, the changes in the pelvis are very marked. In some cases the entire pelvic lining was practically necrotic, lifted from its bed by hemorrhage. After twenty-four hours there is marked hydronephrosis and tremendous infiltration with polymorphonuclear leukocytes.

After forty-eight hours there are very definite signs of repair, not only phagocytosis but connective tissue proliferation, in an attempt to repair the damage that has been done. In the peripelvic tissues there are great masses of polymorphonuclear leukocytes; in some areas there is a marked increase in the macrophages which are filled with granules and portions of red blood cells which have been destroyed.

After seventy-two hours there is considerable clearing up of the peripelvic tissues. There is definite hypertrophy of the connective tissue and attempts at healing. After ninety-six hours, abscesses are formed because of the hemorrhage and infiltration with pus cells. When normally there is loose areolar fat tissue, there is thick connective tissue. After five days in some instances the hemorrhages have been absorbed to a considerable extent. In other instances there is evidence of thick connective tissue. Even after two weeks there are some cavities lined by an inflammatory membrane connected with the pelvic cavity.

DISCUSSION

DR. ANDREWS: Did you do any experiments when the ureter was tied for a certain length of time and then released?

DR. HELMHOLZ: No. All of these experiments were carried out in one way, as it was our object to see what the acute changes were following tying of the ureter.

DR. MYERS: Did you ever have occasion to find out what would happen if you had an infection of the blood stream and tied off the kidney?

DR. HELMHOLZ: We have performed a large number of experiments in which bacteria were injected into the circulation after one or both ureters were tied, and we find that it takes a considerable period of time for them to go through into the hydronephrotic sac. It will depend somewhat on the bacteria injected. Usually bacteria appear in the sac in from six to eight hours.

DR. DICKSON: Would you expect somewhat comparable results with a long continued partial obstruction, that is, sufficient to obstruct a normal amount of flow?

DR. HELMHOLZ: I do not know.

ACUTE INFECTIONS OF UNUSUAL SEVERITY. Presented by DR. S. AMBERG.

Within the last year we have had several cases of a very distressing nature, which have had certain features in common and which we think are worth presenting.

Last February, a child, aged 9 months, previously well, started in with vomiting which lasted for half a day. Later, an insignificant bowel disturbance appeared. Pallor developed very quickly. There was a pharyngitis of moderate degree. The child became very toxic and very desiccated. The respiration was fast and relatively deep. The pulse was very rapid. The leukocyte count was 11,000. The temperature rose to 106 and then to 108 F. The child became limp and hypotonic. Two days and a half from the beginning of the illness, he died.

In the second instance, the child, aged 2½ years, was in excellent condition before becoming ill. The child started with vomiting and developed the symptoms indicated in the previous case. It was impossible to get into a vein to get blood for a culture. The child was brought to the hospital in the evening after having been moderately ill during the day. The main features in the case were the same as in the first case. In this particular instance all the events occurred within eighteen hours.

The third patient was 11 months old, and before being taken ill was in excellent condition. He had been exposed to scarlet fever. The attack started with efforts at vomiting. Although there was no rash or no definite reddening of the throat, the physician made a diagnosis of scarlet fever and sent the child to the isolation hospital. The throat was but slightly reddened. There were symptoms of overwhelming infection as evidenced by pallor, limpness, stupor, coma and sunken eyes. The temperature was only 101 F. two hours before death. The possibility of edema of the brain was considered, and a lumbar puncture was done, 30 c.c. of fluid being removed.

Necropsy was performed on these three patients, but no adequate cause of death was found. In the first instance there was some edema and degeneration of the brain; in the second, the thymus weighed 37 gm., and there was general lymphoid hyperplasia; in the third, there was a very marked edema of the brain and the suprarenal glands were rather small. Our diagnosis in each case was an overwhelming infection.

We had another case of special interest, for it may readily belong to the same group of very severe infections, although it did not result in death. This patient was a boy, aged 3 years, who started in with vomiting and frequent bowel movements, but nothing of unusual severity. When seen on the fourth day there was pallor, cyanosis, and a great degree of toxicity. The pulse was fast. The child was immediately sent into the hospital. There was a pharyngitis of moderate intensity and one ear drum was slightly reddened. By evening the pharyngitis became severe and the throat intensely swollen and injected. Extensive ulceration of the buccal mucosa occurred. A blood culture showed a hemolytic streptococcus.

Attention should be called to the frequency of localized gingivitis and stomatitis as first findings in various febrile conditions. The mucosa of the mouth, and possibly of the nose, may perhaps serve repeatedly as portals of entry in cases in which hitherto a focus of infection has been blamed.

DISCUSSION

DR. MYERS: Did you have blood cultures taken in all cases?

DR. AMBERG: One of the patients unfortunately was moribund before we could get any cultures. A culture was obtained in the last patient, but has not yet grown.

DUODENAL ULCER IN THE NEW-BORN INFANT. Presented by DR. R. L. J. KENNEDY.

The pathologic findings in a case of melena neonatorum were presented. This case was unusual in that there were evidences of early healing of duodenal ulcer. In this ulcer and in ulcers from two previously reported cases, streptococci were demonstrated microscopically in the tissues. (This paper is to be reported in detail very soon.)

DISCUSSION

DR. HELMHOLZ: These three cases are of unusual interest in demonstrating the relationship of melena of the new-born and duodenal ulcer. In the past, we have assumed that melena was due, first, to an ulcer somewhere in the gastrointestinal canal and, secondly when no ulcer was found, to oozing from the mucous membranes somewhere in the gastro-intestinal canal. The difficulty in finding the ulcer is such that I feel sure that unless serial sections are made of the duodenum, the likelihood of its being overlooked is great and the bleeding will be ascribed to oozing. I do not believe that we would have found this ulcer without serial sections. There was a hemorrhage in the duodenum which we thought might be the ulcer, but it later was proved not to be an ulcerated area. The rapidity with which these ulcers heal shows that the ulceration may heal before the patient dies.

DR. SCHLUTZ: Did these patients have any pronounced constitutional symptoms that would enable you to determine the type of condition?

DR. KENNEDY: I think Dr. Helmholz really doubts that there is true melena neonatorum which is not due to an ulcerative lesion. Of course, the severe cases of melena are usually markedly symptomatic of melena toward the end.

DR. TAYLOR: I have had an opportunity to observe one patient who had normal bleeding and coagulation times, but who died because of melena and who had a rather large ulcer, as large as the tip of my little finger. Could it not be that there are two types of melena, the rather rare duodenal ulcer without associated hemorrhagic disease of the new-born, and hemorrhagic disease of the new-born without ulcer?

DR. KENNEDY: There was undoubtedly bleeding before death, and with this mass of granulation tissue there is no reason to suppose that bleeding would not have continued. The central part was undoubtedly not healed and granulation tissue of that type could bleed, as Dr. Mann reports.

QUESTION: Did your patient have a particularly prolonged bleeding time?

DR. KENNEDY: Yes. This is the only instance in which this condition has occurred. Thiele reports sixty-four cases, none of which showed a coagulation or bleeding time longer than normal. His idea is that the so-called hemorrhagic diathesis is not a cause of true melena.

DR. MYERS: Do you think it possible by means of a barium meal to demonstrate the presence of an ulcer?

DR. KENNEDY: I do not think there would be enough deformity in such a young child. It does not appear as if the technical difficulties would make this possible.

XANTHELASMOIDEA. Presented by DR. M. G. PETERMAN.

The patient, a girl, aged 5 years, had been on the ketogenic or high fat diet for three months with almost complete freedom from epileptic attacks. One week before the last visit to the Clinic, the mother had noticed a slight yellowish tinge of the skin. On the following day several small red papules appeared on the face and right arm, later appearing over the trunk and the extensor surfaces of the extremities. Twenty-four hours later the papules became a deep canary yellow. Three crops of lesions occurred, associated with intense itching.

On examination, the skin of the entire body showed a slight yellowish tinge. The sclerae and the mucous membranes were normal, as were also the eye-grounds. Scattered groups of papules, varying from the size of a pinhead to that of a pea, covered the entire body and extremities. The tops of many lesions had been scratched off. A bee sting on the left cheek and a superficial scratch on the right arm were tinged yellow.

The physical examination otherwise was negative. The stools and urine were normal in color. The blood serum contained no bile pigment but was lipemic, the total fat content being 577 mg. per hundred cubic centimeters.

The diagnosis of this condition lay between an unusual colored xanthelasmoidea (urticaria pigmentosa) or a xanthoma tuberosum.

DISCUSSION

DR. SCHLUTZ: Is the patient getting any treatment besides dietary therapy?

DR. PETERMAN: There is no drug therapy. The patient is getting no carrots or oranges. There was nothing in the food to which we could attribute this difficulty.

DR. STEWART: How long has this discoloration lasted?

DR. PETERMAN: The patient has just left the Clinic.

DR. SCHLUTZ: Was there any itching?

DR. PETERMAN: Considerable itching at the beginning of each crop of lesions.

DR. TAYLOR: Provided this is xanthelasmoidea, what is the outcome?

DR. PETERMAN: Xanthelasmoidea usually persists until puberty. It may disappear then.

DR. TAYLOR: It is a disease with which I am not familiar. Does it disappear and return at intervals?

DR. PETERMAN: Crops of papules will continue to return with any injury or trauma.

Book Reviews

THE PECULIARITIES OF DISEASES OF THE EYE IN CHILDHOOD. By PROF. L. HEINE, KIEL, Abhandlungen aus der Kinderheilkunde und ihren Grenzgebieten, Beihefte zum Jahrbuch fuer Kinderheilkunde. Heft 6. Herausgegeben von A. Czerny. Pp. 52, with 9 illustrations. Berlin, S. Karger, 1925.

The treatise opens with a clear and succinct presentation of eye embryology and anomalies of development, then takes up the diseases of the different anatomic divisions in much the usual order — lids, conjunctiva, cornea, iris, etc. The last twenty pages include a discussion of the special refraction, accommodation, binocular vision, muscle and pupil disturbances peculiar to childhood, and special chapters on scrofula, tuberculosis, syphilis (especially hereditary syphilis), injuries as they affect the eye of the child, and lastly a number of pages on eye conditions met by the school physician and teacher, including poor vision, "batting" of the eyes, oblique position of the head, tearing of the eyes, spots before the eyes, poor body position and headache.

The presentation is made from a practical, sane and healthy point of view; it avoids most controversal matters, is sufficiently detailed, yet never too much so, and above all the pages are full of the writer's own experiences, he does not draw on others largely for his data, he presents his own. Among interesting matters one finds the following, new and old: The growth of the eye is completed "in principle" in the second month. Phlyctenular disease often leads to myopia. Both the spinal fluid and blood Wassermann tests are negative in 50 per cent. of keratitis interstitialis and hereditary syphilis, even in the presence of Hutchinson's teeth, poor hearing, swollen joints, peripheral chorioretinitis or similar complications, and the more stormy the course the better the vision eventually. Nasal conjunctivitis is so characteristic of congenital stoppage of the tear duct that it is surprising how often it is overlooked. Disseminated chorioiditis in children is mostly tuberculous. Cerebrospinal meningitis is the main cause of panophthalmitis in children, and may occur without any general symptoms of meningitis. It is a question whether or not the slightly enlarged eye so often found at birth is really ever without other pathologic changes. When the cornea is beyond 10 to 11 mm. in diameter, "the parents marvel" but the doctor should think of congenital syphilis. It may be the only anomaly.

Lamellar cataract is the most frequent lens disease in childhood, and is due to toxins and endocrine disturbance, and possibly to a lack of vitamins. It is usually stationary, and when vision is reduced one-half in males or to one-third or one-fourth in females, a stenopeic iridectomy downward will adequately improve vision. Glioma is difficult to distinguish from pseudoglioma, but it is better to take out the latter eye than leave the former. No child who squints should be sent to school, but the sight should be corrected before school age by glasses or by operation. With Czerny, he considers scrofula to be a lymphatic diathesis with a disposition to react in a certain way to outer insults, especially "formed ones" and to differ from a real tuberculosis. The latter plays a less significant rôle in childhood than does scrofula, while the reverse is true in adult life. Sympathetic ophthalmia has a more serious prognosis in childhood. Do not take out the injured eye while it has vision, for "many" times it retains better vision than the sympathizing eye.

If the average good pediatrician can read this book with as much profit as can the average good eye doctor, it will serve a useful purpose.

PEDIATRIC NURSING. A TEXTBOOK FOR NURSES. By ABRAHAM LEVINSON, B.S., M.D., Associate in Pediatrics, Northwestern University Medical School. Cloth. Price, $2.50. Pp. 251, with 28 illustrations. Philadelphia: Lea & Febiger, 1925.

In this little book, Dr. Levinson has presented most of the important facts about infants and the diseases of childhood in a very trite manner. He has been happy in his synopsis, and has presented each subject as briefly as is conceivable.

His chapter on "The Kind Grandmother"—how to win over the grandmother, and when to overrule the grandmother gives many practical and unique suggestions.

Most of the illustrations are good, and the book undoubtedly will be a helpful reference book for nurses.

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